

No Tax on Books and Papers

In April 1940 the Chancellor of the Exchequer announced the introduction of a purchase tax on certain goods. Among these were books. A campaign against this move was immediately started by publishers and a broader base of support rapidly developed. A deputation led by the Archbishop of Canterbury and including Sir Arthur Eddington and Professors A. V. Hill and R. H. Tawney tried to persuade the Chancellor to change his mind. When this failed, the Archbishop, Mr J. B. Priestley and Sir Geoffrey Faber pleaded with MPs for support. This was forthcoming, and in August 1940 the Chancellor announced the exemption of books from tax. The principle that books are not taxed has held since.

When Value Added Tax (VAT) replaced Purchase Tax and Selective Employment Tax in Britain, the principles were re-asserted. VAT (which, it has been said, should more correctly be called SPIT, for selling-price increase tax) is not levied on books, nor on newspapers and periodicals, nor (among other things) on food. The zero-rating on printed matter is not part of a concession, say, to scientific and medical research (water is zero-rated, distilled water is not!) nor to the academic community; it is a clear affirmation of the importance attached to the printed word. *Private Eye* and *Men Only* are zero-rated alongside *Nature* and the *Oxford English Dictionary*.

A problem, however, is fast approaching, and was given wide publicity by Mr March Hunnings in the *Times Literary Supplement* of August 31. There will be strong pressure within months in the EEC for unified VAT rates. Other countries in the Common Market do not zero-rate books, so if unification is done on a majority basis Britain will be expected to raise the rate to at least 5%. British diplomatic efforts are likely to be fully extended in attempting to keep food zero-rated.

The case for no taxation is as valid in 1973 as it was in 1940. Books and papers still live on the margins of most personal budgets—as desirable possessions but amongst the first to be jettisoned if money becomes tight. Furthermore, it will be the poorer, to whom the cost of books and papers represents a larger fraction of their income, who will suffer most. If the tax goes up on most consumer goods there is the possibility of a change in habits to settle for less. This is not easily done with printed matter—the choice is between buying and not buying.

The present zero-rating on printed matter is an assertion of the importance of thinking and participation. A clear line is drawn between, for instance, printed music (zero-rated) and gramophone records (rated at 10%); between books (zero-rated) and television sets (10%). This is an enlightened attitude for a Government to take, especially as it is thereby denied of substantial revenue. It is, one hopes, not utterly starry-eyed to say that the absence of tax on printed matter ought to be maintained simply because it makes Britain a more civilized place.

What tactics should be adopted to attempt to retain things as they are?

Those in the publishing business can be accused of

being motivated by self-interest; thus any organized opposition to such tax moves would have to be as broadly based as it was in 1940 to carry deep conviction, and it would have to be seen not to be a vehicle for another attack on Britain's membership of the EEC. Whereas representatives of trade unions, staunch defenders of the printed word, would provide eloquent support, their implacable stand on the EEC might prove an embarrassment. On the other hand, few distinguished scientists have revealed strong European prejudices. They would be admirable members of any opposition movement.

It should be said that such a movement would have to work within a European framework. There would undoubtedly be much sympathy in Whitehall for it, but the question is an international one and other countries within the EEC should be made aware of the depth of feeling. Two courses are possible. A case could be made that Britain should be allowed to continue as an exception in zero-rating. But a more imaginative approach would be to urge other countries to come into line with Britain (probably by exemption rather than zero-rating—an exquisite difference). There are reasons to believe the latter is the right way to go. It has less connotations of Britain as the loner and is thus not seen as a threat to EEC unity. Newspapers are already exempt in some countries. It could be a valuable boost to the as yet poorly developed concept of cultural benefits springing from European unity, by means of a levelling up rather than down of civilizing assets. It would be an excellent opportunity to make new contacts in Europe. And most obviously, it would, if successful, be good for everyone.

The question of VAT-rating is not a narrow domestic issue. If handled intelligently it could have broader European benefits. Moves towards VAT which President Nixon has made imply that now is also the time to raise the issue of exemption in the United States.

100 Years Ago



The *soirée* in St. George's Hall last Thursday was a great success; indeed all the arrangements for the meeting have been satisfactory. The public lectures, by Profs. W. C. Williamson, Clerk-Maxwell, and Dr. Siemens were well attended, but the proportion of the working-classes present at the lecture on Fuel, which was specially intended for their benefit, was very small.

From the report on the British Association meeting at Bradford
From *Nature*, 8, 448, September 25, 1873.



OLD WORLD

NERC Foresees Difficulties over White Paper

THE Natural Environment Research Council is facing "serious difficulty" in attempting to meet the transfers of funds to government departments which are required following the publication last year of the white paper *A Framework for Government Research and Development*.

In its annual report published this week (House of Commons Paper 426, HMSO, £1.20) the council states that "it will not be difficult to meet the first year's transfers (for financial year 1973-74) with applied research projects of direct relevance to departmental interests". But "the possibility can be foreseen from experience of the first year of transfer, that really serious difficulties will arise in later years in fitting NERC programmes, scientific skills and facilities to departmental responsibilities...".

Under the terms of the white paper, £2.55 million was transferred from the council's budget to the customer departments in 1973-74, with a further £3.6 million and £4.8 million due to be transferred in 1974-75 and 1975-76. NERC's customers are the Department of Trade and Industry, the Department of the Environment, and the Ministry of Agriculture, Fisheries and Food.

The council goes on to warn that if the various needs of the customers and of fundamental research are not properly coordinated, the scientific capacity of the country in some fields could be reduced "to a damaging degree".

The difficulty, the council says, is that sometimes two or all three of the customer departments "are concerned with different applications from a field of research that cannot be sensibly subdivided. This difficulty will increase in attempting to meet transfers for the second and third year".

Areas that are likely to be hardest hit in this way are the Geological Survey and practical research in coastal waters—storm surge prediction, coast protection and offshore navigation.

"For these and other fields, which also include a significant amount of fundamental research, it will be necessary to devise a system whereby the various customer requirements and the needs of fundamental research are properly dealt with in a coordinated way."

But even so it is possible that "really serious difficulties" will arise in the second and third year, in trying to fit NERC programmes to departmental needs "in such a way as not to destroy

the balance of fundamental and applied research in many of the sciences of the natural environment. If this were to happen it would reduce the scientific

capacity of the country in some fields to a damaging degree".

The council highlights its problem by pointing out that the £4.5 million

Transfer of NERC Funds			
Recipient	1973/74	1974/75 £m at 1971-72 prices	1975/76
DTI* DOE MAFF NCC	1.25 0.75 0.25 0.30	1.85 1.15 0.375 0.30	2.50 1.50 0.50 0.30
for commissioned R & D			
Sub-total	2.55	3.675	4.80
NCC (conservation)	1.1	1.1	1.1
TOTAL	3.65	4.775	5.90

* DTI—Department of Trade and Industry; DOE—Department of the Environment; MAFF—Ministry of Agriculture, Fisheries and Food; NCC—Nature Conservancy Council.

IONOSPHERE

Coherent Project

by our Astronomy Correspondent

THE Science Research Council is being asked to help support a £3-4 million European ionosphere project. This week a group of British ionosphere scientists is applying to the SRC for £18,000 to pay for a design study of a VHF transmitter which, if built, will be the British contribution. It will probably be several months before the decision of the SRC is known, but it is believed that both the council's Geophysics Working Group and Space Policy and Grants Committee have expressed strong support.

The plan calls for the construction of an ionosphere sounding station at Tromsø in Norway which will be able to determine as many as fourteen parameters of the polar ionosphere from a height of 80 km up to 1,000 km. The station will operate on the incoherent scatter technique in which a radio beam directed vertically upwards causes the free electrons of the ionosphere to oscillate and thus radiate a radio wave of approximately the same frequency as the original signal. Because of the small scattering cross-section of electrons and the fact that the scattered wave is emitted in all directions, the signal received back at the ground is weak and so powerful transmitters have to be used.

Other contributions to this programme—known as the EISCAT project—are to come from France (a UHF transmitter), West Germany (the UHF aerials), Finland (a VHF aerial), Nor-

way, possibly Sweden and possibly the Soviet Union. Negotiations have reached different stages in the various countries. In France the design study for the UHF transmitter is complete, and there is thought to be a possibility that funds will be available from 1975. It is believed that the French would favour four equal contributions from France, West Germany, Britain and the Scandinavian countries. In West Germany the design study for the UHF aerials is virtually complete, and although the West German government does not wish to support the project it seems that the Max Planck Foundation may be able to help. The Norwegian Research Council and the Norwegian Physics Council have both expressed support for the project, and Finland is carrying out a design study for the VHF aerial.

The Soviet contribution would be a UHF receiving station near its border with Norway, and it is believed that this project has been approved by the Academy of Sciences although so far there has been no official approval from the Soviet government.

British ionosphere scientists feel that it is high time Britain became involved in the project. The existence of another high-latitude incoherent scatter station which is already in operation at Chatanika in Alaska is said not to detract from the need for the EISCAT project. Although the Chatanika station is less sophisticated than the proposed EISCAT project, the data which it has already produced are said to show how much exciting work can be done in the auroral zone using the incoherent scatter technique.

(1971-72 prices) that is to be transferred by 1975-76 represents, on the face of things, 27% of the council's 1971-72 budget of £16.4 million. But, the council goes on, by the time a further £1.1 million has been transferred to the new Nature Conservancy Council and the £2.7 million spent on research training, the £1.5 million spent on the British Antarctic Survey and the £0.3 million spent on the Geological Museum are deducted as these all lie outside the responsibilities of the three customer departments, the budget from which the £4.8 million has to be transferred is only £10.7 million. In other words the £4.8 million which is to be transferred represents 45% of the budgets of NERC institutes.

One solution to the difficulty that the council is facing in transferring programmes to ministries—although not a solution that is proposed in the annual report—might be to alter the balance of transfers between departments. At present the Ministry of Agriculture, Fisheries and Food will only spend £0.5 million with the council by 1976, yet much of the marine and fisheries work undertaken by the council could easily and logically be funded by MAFF. Equally, marine sounding work could be financed by the Ministry of Defence (on a non-secret basis), thus reducing the amounts that will have to be transferred to the budgets of the Department of Trade and Industry and the Department of the Environment.

Apart from outlining its problems stemming from the white paper, the annual report also exhaustively explains the large scale reorganizations that have taken place within the council. The reshuffling of the physical marine science institutes into the Institute of Oceanographic Sciences is expounded and the thinking that lies behind the proposed Institute of Terrestrial Ecology is set down.

The council records its doubts about the move of the administrative offices to Swindon, which will possibly be completed by 1977, leaving only conference facilities and office services for senior employees in London. It is the view of the NERC Staff that dispersal will "seriously weaken the coherence of NERC as an organization".

GRADUATE EMPLOYMENT

Better Prospects

A DOUBLE warning against over reaction to short term trends in higher education was delivered in Dundee last week at the Standing Conference of University Appointments Services.

Lord Boyle, Vice-Chancellor of the University of Leeds and a former Conservative minister of education, informed the conference that the fact

that the situation for graduates seeking employment is much easier this year than last (there are now about 20% more vacancies) underlines the danger of drawing long term conclusions about the future of university courses and of graduate careers on the basis of short term statistics.

Sir Kenneth Berrill's version of the same warning was a somewhat more sophisticated one. Speaking for the last time in public as Chairman of the University Grants Committee (he becomes chief economic adviser at the Treasury in October), Sir Kenneth outlined the difficulties and doubts that beset a chairman of the UGC.

Quoting the government's target of 750,000 students in higher education by 1981 (half of them in universities and half in polytechnics), Sir Kenneth said that planning for each subject that will be studied in universities by then was not easy. Attempts to define the different types of skill that will be needed in 1984 are a waste of time. Relatively few people go into careers that follow directly from their degrees.

Equally, unemployment among graduates is difficult to forecast and the biggest danger lies in reacting too quickly. When a bad year occurs, as in 1971, nothing can be done immediately to rectify the situation. The results of any change will not be seen until several years later.

Two basic difficulties beset planning for 1984. The first is that the system may not react at all to change and, paradoxically, the second is over reaction, or as Sir Kenneth terms it, the "bandwagon effect".

Changing the ratio between the arts and sciences in universities from 55 science to 45 arts to 53 to 47 by 1976 means that for every new place provided in the sciences two have to be provided in the arts, and this is difficult in a system in which until recently the emphasis was the other way around. On the other hand the system can over-react because it is so decentralized. At present, Sir Kenneth said, universities are asking for expansion in biochemistry, pharmacy and biology—the move towards the life sciences. But universities all over the country are thinking the same way, and there is a danger that too many courses will be started.

Equally, when Lord Ashby as Chairman of the Royal Commission on Environmental Quality asked the UGC to conduct a survey on university teaching in pollution matters, the survey revealed that an enormous number of universities had moved with the times and introduced work on the subject into their courses.

When the university appointments officers at the conference were not being lectured on future trends in graduate employment, they were busy

discussing the current situation. Chiefly they conclude, in the absence of final figures, that this year has been much better than last, which in turn was an improvement on 1971. The most notable trend is that many officers report that while industry has vacancies to offer, an increasing number of graduates are not interested in taking up the jobs. At the end of the year many predict there will still be jobs in industry going, and there will still be undergraduates on the "unemployed" list. More and more graduates want to look around before taking a job, and there is some evidence that industry in particular is under suspicion for its actions in 1971 when, in some cases, offers of jobs were withdrawn after they had been made. Now that the situation is brighter, and GEC, for example, has the better part of 600 graduate vacancies, many graduates do not want to know.

POLITICS

Shortage of Science

THE scientific community owes a debt of gratitude to the National Association of Conservative Graduates. Out of 1,304 motions to be debated at the Conservative Party annual conference to be held at Blackpool on October 10-13 the one and only motion to do with research and technology is proposed by this association. The Labour Party's agenda of 436 motions for their conference on October 1-5 contains no such item. The Liberals also had little time for science although energy policy was discussed on Wednesday afternoon of this week at their conference at Southport.

The Conservative motion asks the conference to deplore "the continued waste of money on inadequately founded national ventures in scientific research and in technology". However, the remainder of the motion calls for such projects (presumably not inadequately founded) to be "pressed forward in future on a multilateral or European basis".

Energy policy and environmental planning get a great deal of attention in the manifestos. The Labour Party is called upon by its members to implement an energy policy and also to establish a "working party to evaluate present energy resources and to consider ways of ensuring state exploration of all forms of energy". The Liberals called this week for a permanent energy commission to be established to advise the government and they also asked for an assessment of the future of nuclear energy, taking into account reactor safety, polluting effects and "the moral justification for storage of wastes for future generations to deal with". The Conservatives will not debate energy

policy *per se* but the representatives from East Dudley ask the conference to "view with concern the pending exhaustion of some of the natural resources of our overcrowded Islands and to look to the government for an enlightened strategy for those resources and for population".

Higher education does not receive much attention from the Conservatives or the Labour Party but the Liberals on Friday morning will be discussing education from the age of 16 onwards. But the few resolutions on this topic are in a familiar vein. The Conservatives are to be asked to make student loans repayable "over a reasonable period, or on emigration, or by undertaking two years approved civic or social work".

The Labour Party conference will be asked by the National Organization of Labour Students to abolish the system of discretionary awards and to provide maintenance awards at full value to all students in higher education. A novel motion in the Labour Party agenda this year is a call for all workers to take a year's "sabbatical" every fifteen years—at full pay, of course.

PARTICLE CONFERENCE

Need for Exposition

from *La Recherche*

THE second Aix-en-Provence International Conference on Elementary Particles ended on September 12 after a week's review of new developments in particle physics. Attended by more than 600 physicists from (almost) all over the world, the colloquium was, in fact, the seventh in a Europe-wide series begun in Aix in 1961 and it was organized by the European Physical Society and the Société Française de Physique. This year's meeting had a few sideshows, not all connected with particle physics, of both the planned and unanticipated varieties.

The scientific content of the conference was straightforward and without surprises*. But it was the social and even political appendages which made things livelier than usual. In an era when subatomic physics is still not clearly understood by nonspecialists, the organizers and the French hosts had the good sense to schedule some popularization sessions at first called "About Particles and Physicists" but later transformed conveniently to "Aix-Pop"—a series of end-of-day encounters

* There were sessions on the electromagnetic production of hadrons, hadron spectroscopy, hadron decays, neutrino interactions, strong interaction theory, unified theories of weak and electromagnetic interactions, new trends in field theory, elastic scattering and low multiplicities, high multiplicity reactions, large transverse momentum phenomena, and 400 GeV physics. Briefer sessions were devoted to weak interactions and neutral currents.

between physicists and local citizens. High energy physics was explained from A to Z—for those who wanted to know—mainly in the open court of the stately seventeenth century Hôtel Maynier d'Oppède mansion.

There, under the shade of enormous plane trees, the man or woman in the street could wander in and browse among static or working models of accelerators, bubble chambers, spark chambers and cloud chambers. There was also a demonstration to explain quarks. Also explained or contested were antimatter, the ecological and military aspects of nuclear energy, research and its relation to economic growth and the research needs of the developing world. The people who came off the street to see the exhibits (and operate some of them), as well as to meet theoretical and experimental physicists in the flesh, were those one would expect: the ones who venture to the theatre, a concert or an art gallery. The working man's social stratum was not represented in these encounters at Aix, so next time the organizers will use a new approach in trying to educate the public in high energy physics. They will go to residential and shopping neighbourhoods to make contact, according to Michel Crozon of the Collège de France.

Why this pre-occupation with the popularization of something assumed to be arcane to the nonspecialist? Professor Victor Weisskopf of MIT perhaps explained it best when he lamented that astrophysicists and radio-telescopicists always seem to command public attention while the layman simply has not been stimulated by anti-neutrinos, hadrons and pomerons. "Imagine", visualized Weisskopf, "carrying on an enthralling conversation with a layman about neutral currents. We are to blame: we spend too much effort in trying to publicize the latest findings and theories".

Coming Shortly

THE latest television programme in the series which has included *The Violent Universe*, *The Mind of Man* and *The Restless Earth* has just been completed. It is written by Nigel Calder and called *The Life Game*, and will be shown in the Netherlands on September 24, Belgium on September 25 and 26, Canada on September 30, Australia on October 3 and Britain on October 13. Dates for showings in Germany, Sweden and the United States are not yet available.

In *Nature* on October 12 Nigel Calder will write on the problems of presenting science as intellectual entertainment.

Weisskopf also pointed out that one of the world's most prestigious journals dedicated to making science popular "publishes one article every two years on high energy physics, whereas we have about 10–15% of the total civil research money in the world. Yet scientists and science writers have no problem in bringing out articles on continental drift one after the other. It's our job to make our own work known to the rest of humanity".

The People's Republic of China was represented for the first time in this series of conferences. The three-man team from Peking was headed by Professor Chung Wang, director of the Institute of Atomic Energy. The Chinese, who were *en route* to their homeland after a week's visit to Stony Brook and the Batavia research institutions in the United States, presented no papers although Professor Wang served as chairman of the session on neutrino interactions.

Physicists from Australia or New Zealand were, however, not officially present at the Aix congress. An unofficial observer, from the Australian National University at Canberra, charged publicly that French visas had been denied to Australian and New Zealand scientists wishing to attend the conference, presumably because of the currently strained relations emanating from the French nuclear testing at Mururoa Atoll. But the meeting's official organizing committee adamantly and repeatedly denied that there had been official interference by the French government in regulating attendance by New Zealanders or Australians.

Aix has recently felt ripples of the racial antagonism between natives and imported North African labourers in nearby Marseille and a petition was circulated at the meeting, asking men and women of the world of research to condemn racism. At least a hundred signatures were collected. Meanwhile, the French Communist Party unit at the Cadarache Nuclear Research Centre circulated broadsheets to conference participants fixing the responsibility on scientists and engineers for pollution, spoilage of the environment and the subservience of man to machine. "Only socialism can master our economic growth", proclaimed the flyer.

Summing up the trials and tribulations of the particle physicists in their general relationship with the other sciences, governments and the public, CERN's D. Amati hypothesized that "Possibly we are too institutionalized as professional scientists". He suggested that high energy physicists become more flexible in their dealings with people outside their discipline. Commented Weisskopf, "I would like to think that you are wrong, but I believe that you are right".

NEW WORLD

Clean Air or Warm Homes?

by our Washington Correspondent

A YEAR ago, the environmentalist movement in the United States was able to point to a series of spectacular achievements and stunning victories over the federal government and other despoilers of the natural environment. Among its more prominent victims it could count the Alaska pipeline, which had been held up for three years by legal tangles; the Atomic Energy Commission, which had been forced to consider environmental factors before granting licences for construction and operation of nuclear power plants; DDT, which had been banned; automobile manufacturers, who had been denied their request for an extra year in which to develop clean cars; and polluters of air and water who had been put under the gun by strong legislation passed by Congress. Then came the energy crisis.

Although it would be overstating the case to say that the environmental bandwagon has been derailed by the barrage of publicity and widespread concern about fuel supplies, there is no question that it has lost momentum and that it is facing an even tougher period in the months immediately ahead. A series of setbacks in the past few weeks and impending battles over the development of energy resources attest to that. All of which puts Russell Train, whose appointment as Administrator of the Environmental Protection Agency was approved by the Senate last week, in one of the hottest seats in the federal government.

Train held his first press conference as EPA Administrator last week, and for more than an hour he was faced with a barrage of questions about whether energy policy dictated by the White House would castrate the EPA's drive to clean up air pollution. In particular, he was repeatedly questioned about a meeting held in the White House on September 8, after which President Nixon and Governor John Love, the head of the White House Office of Energy Policy, announced that some air pollution controls will have to be lifted this winter to prevent power blackouts. That decision, perhaps more than any other, is being seized upon as a signal that the environmental movement has come up against the energy crunch.

In short, the White House is putting pressure on state governors to adopt contingency plans to lift pollution control requirements on power plants by allowing them to burn fuels containing relatively high quantities of sulphur if

supplies of low-sulphur oil dry up this winter. Train emphasized that lifting the regulations would be a temporary solution to an acute problem, and that it in no way signals long term relaxation of air pollution controls. In two or three years' time, he argued, the technology for removing sulphur from oil and sulphur dioxide from stack gases will be more widely available, and fuel supplies will be stepped up.

Unfortunately, however, a couple of days before the White House announced the need for relaxing controls, the EPA itself proposed that some controls be lifted on coal burning power plants and copper smelters because stack gas cleaning technology is not widely available. And, last week, officials from oil and gas corporations were arguing, in a set of public hearings concerned with off-shore production of oil and gas, that there is little prospect of a letup in fuel shortages for the next few years. Thus it can be safely assumed that, in the absence of adequate clean-up technology, a trade-off between air pollution controls and oil shortages will have to be faced not just this winter, but for many years to come.

SCIENCE POLICY

Informal Advice

by our Washington Correspondent

SINCE the President's Science Advisory Committee last met in December 1972, before it was abolished by President Nixon, there has been no provision for the scientific community in the United States to have a formal voice in the federal government's science policy apparatus. Last week, however, Dr H. Guyford Stever, Director of the National Science Foundation and now the President's Science Adviser, took the first step towards setting up a mechanism for sounding out the views of the scientific community. He called together the heads of 19 of the largest scientific and engineering societies in the United States to discuss "whether the views, hopes and needs of the professional scientific community can be introduced into the science policy-making process".

The meeting was closed to the press, but Stever said afterwards that there was general agreement that contact between the science adviser and the heads of scientific organizations should be developed. Consequently, Stever said that he will call similar meetings

The Energy Policy Office says that it has not received a deluge of complaints about its proposal, which is probably fair indication of public reaction to the energy crisis. (Indeed, it would be remarkable if there were no public concern about the matter, since the oil companies are spending millions of dollars advertising the seriousness of the situation—ecopornography has given way to thermopornography.) But that is not to say that the office is getting away with its proposal without raising some opposition. Senator Edmund Muskie and his Air and Water Pollution subcommittee is not happy about it, nor is the Natural Resources Defense Council (NRDC), a public interest law group which has fought many a legal battle with the government and won.

NRDC lawyers fired off a letter to Love's office last week, suggesting that his proposal is "a shocking attempt to make Americans' lungs bear the burden of the Administration's failure to take meaningful steps to improve our short-term energy situation". Not only that, but the energy office has acted illegally in failing to produce a statement giving

on an informal, but fairly regular, basis in the future, and he also said that he hopes to be able to incorporate in science policy decisions the work that the societies themselves are doing on such problems as manpower planning. There are also plans to call together a group of representatives from industry in October, to discuss means for bringing the industrial viewpoint to bear on science policy.

For their part, the scientific societies had already begun to consider how they could make the views of their members known to the Washington decision makers, well before Stever called them to a meeting. Early in July, for example, the heads of some 13 societies formed a Committee of Scientific Society Presidents, under the chairmanship of Dr Alan Nixon, President of the American Chemical Society, with the intention of working for "a constructive national science policy". Although the committee has no paid staff and no budget, the newly opened lines to Stever and his staff could strengthen its voice in national affairs. Nevertheless, an informal committee giving informal advice to the science adviser still does not give the scientific community a powerful and continuing voice in the corridors of power.

details of the environmental impact of its proposal, as required by the National Environmental Policy Act (NEPA), the lawyers suggest. Such an impact statement, which is required by NEPA for all government projects having an impact on the environment, should spell out exactly what is being proposed, and alternative methods of approach.

One possible method for alleviating fuel shortages this winter, NRDC suggests, is for the federal government to require some meaningful conservation measures, instead of the almost derisory moves in that direction which have been made so far. Moreover, the letter points out that the energy office has not said which regions will be affected by relaxation of pollution controls, how long they are likely to last, or how great the shortage of fuel is likely to be. For its part, the energy office says that it does not know the answers because they depend on how cold it is going to get.

Already the Congress is putting final touches to legislation which will clear away all obstacles to construction of the Alaska pipeline although environmentalists will probably fight the legislation in the courts on the grounds that it is unconstitutional, and as a last resort they are considering the possibility of bringing an antitrust suit against the companies intending to build and operate the pipeline. And automobile manufacturers have now been given the extra year they want to develop exhaust clean-up technology. But there are at least four other major issues which will be fought out in the next few months. They are strip mining of coal, exploitation of offshore oil and gas reserves, extraction of oil from shale in the Rocky Mountains, and an attempt to weaken the Clean Air Act.

As far as strip mining is concerned, the United States possesses more than half of the world's reserves of coal, and much of the low sulphur deposits lie close enough to the surface to be extracted by opencast mining. Already, whole areas of the Appalachians have been stripped of coal, leaving behind massive destruction of mountainsides, streams and vegetation, and large-scale strip mining is likely to begin soon in the Midwest, particularly in Montana. Although some opponents of strip mining are demanding nothing less than a total ban on the method, the battle lines are being drawn chiefly around bills before Congress which are designed to force coal companies to repair the damage wrought by their coal shovels—the largest of which can scoop up 2,000 tons of soil and coal at a single bite. At issue is the stringency of the regulations requiring the coal companies to fill in and revegetate the scars left on the land. Similarly, proposals to exploit the off-

shore deposits of oil and gas and the Rocky Mountain oil shale fields are being fought chiefly to ensure that exploitation of the energy resources is accompanied by adequate environmental protection.

In the long run, the outcome of the various confrontations between the desire to protect the environment and the need for adequate supplies of energy is likely to depend, in large part, on how Mr Train guides the EPA in the next few months. He is on record with a number of tough speeches criticizing those who have made the environment the whipping boy for the energy crisis, and he has spoken out against the move in Congress to exempt the Alaska pipeline from further review under NEPA. And last week he reiterated his support for the thrust of NEPA and the Clean Air Act and said "I am not a rubber stamp for the Administration". In particular, a critical factor will be whether Train's voice in the White House will be equal to that of Governor Love and his Office of Energy Policy. Differences of opinion are already emerging between EPA and Mr Love's office, and the compromises that will eventually be reached will set the basis for environmental policies for many years to come.

HUMAN EXPERIMENTATION

No More Abuse

by our Washington Correspondent

THE Senate last week voted to set up a national commission to safeguard the rights and welfare of those who take part as experimental subjects in biomedical or behavioural research. The move is a direct response to a number of recent disclosures of total disregard for human rights in some research projects, perhaps the most notorious of which was the so-called Tuskegee study of the effects of syphilis, in which treatment was withheld for 40 years from some 200 poor black men who were known to have the disease. The Senate decreed that all grants and research contracts should be subject to peer review before they are awarded by the National Institutes of Health or the National Institute of Mental Health. The Senate also called for a thorough study of the ethical, legal and scientific implications of psychosurgery, and voted to ban research on living fetuses—at least until the proposed commission had a chance to study the matter.

A commission to protect the rights of experimental subjects was proposed by Dr Bernard Katz of Yale University during hearings held by Senator Edward M. Kennedy's Health subcommittee, and it was written into a research training bill by Kennedy and his committee. Made up of eleven members appointed by the President and drawn

from a variety of disciplines, the commission would be charged with the task of drawing up mandatory regulations governing all clinical research supported by the Department of Health, Education and Welfare (HEW). The commission would eventually oversee the implementation of the regulations.

In short, the commission would establish guidelines for the selection of subjects and for obtaining their consent to take part in biomedical research projects, and it would draw up risk-benefit criteria for deciding whether individual research projects are justified. The commission would also be required to recommend to Congress sanctions that can be invoked if the regulations are violated, and suggestions for compensating individuals who are injured as a result of their participation in a research project. Although the bill stipulates that the commission would be concerned only with research funded by HEW, it also suggests that the commission should consider ways to bring all human experimentation in the US under its purview.

A key component of the proposal is the setting up, in every institution receiving HEW funds for clinical research, of institutional review boards which would be certified by the commission. The chief function of the boards would be to ensure that the regulations are properly implemented at the working level, and if necessary they would refer disputes to the commission for arbitration. Every institution receiving funds from HEW for clinical research would be required to set up review boards.

As for the other provisions in the Senate bill, like the House version of the legislation, it calls for some \$208 million to be spent on biomedical research training grants in the present fiscal year. This is in contrast to the Administration's recently announced decision to spend only \$30 million this year on a new training programme, and eventually to build up the expenditure to some \$90 million in three years' time. Whatever Congress finally decides to vote, however, it can be assumed that the Administration will release only what it wants to spend.

Finally, the bill includes a provision demanding that all grants and contracts awarded for biomedical research should be subject to peer review. The provision was included in the bill in response to suggestions earlier this year that the Office of Management and Budget had the knives out for the peer review system because it made the allocation of research money insensitive to central management control. Those suggestions caused such an outcry from the scientific community, however, that wholesale butchering of the peer review system now seems unlikely.

NEWS AND VIEWS

Neutral Current in Weak Interactions?

GARGAMELLE was Gargantua's mother. She had a dreadful and Rabelaisian labour before finally bringing her great child into the world. Nowadays Gargamelle is a giant heavy-liquid bubble chamber at CERN. A vast collaboration of physicists from seven European laboratories—Aachen, Brussels, Milan, Ecole Polytechnique, Paris, Orsay and University College, London—has been acting as midwife to the delivery of her most recent result (presented at the conference on neutrino physics held last month in Bonn). In this case the labour has also been long, not because the offspring was caught up in her internal workings, but because the data were embedded in background.

The chamber was exposed to a neutrino beam and to an antineutrino beam. The kind of events which were expected always includes a fast charged muon in the final state, along with strongly-interacting pions, protons and neutrons from the breakup of the struck nucleus. The process of changing the incident neutrino into a charged final muon is called a "charged-current" interaction. But in Gargamelle more than 160 events have been seen which look exactly like charged-current events, except that there is no muon in the final state. It is impossible to prove for any of these events, taken by itself, that it was a neutrino interaction, but no alternative explanation has been found which could account for even one quarter of the number of events seen. A long list of background processes has been investigated (as described by Hasert *et al.* in a forthcoming issue of *Physics Letters*) but none can reproduce the observed properties of the sample of events, either qualitatively or quantitatively. For comparison, about 570 charged-current neutrino events were seen in the same film, showing that the neutrino flux was more or less as expected.

If it is accepted that most of the 160 events were induced by neutrinos, then the most attractive explanation is that they are "neutral current" events, in which the incoming neutrino or antineutrino has scattered inelastically, but kept its identity. The old-established theories of weak interactions forbid this, but a family of new theories, due to Weinberg and others, requires such neutral currents. These new theories not only attempt to explain the weak interactions more fully; if successful they will establish that the weak interaction and the electromagnetic interaction are two aspects of the same force.

Some properties of the weak interaction are very analogous to electromagnetic interactions at the most fundamental level. Both weak and electromagnetic processes are, for instance, described in terms of currents, a concept of quantum field theory which is remotely related to the everyday electric current. But calculations of weak processes have been very crude because the theory could not be "renormalized". Renormalization is the formal technique which removes infinities and other nonsense properties from the theory of quantum electrodynamics and allows exact calculations to be made for electromagnetic processes. The new theories attempt to renormalize the weak interaction too, but in doing so they predict hitherto unobserved phenomena. In order to cancel out infinite terms from the crude conventional

calculation of weak processes, other unconventional infinite terms must be introduced. These terms are not just mathematical tricks. If they are present they will give rise to one or two physically observable properties; neutral weak currents of the kind Gargamelle has probably discovered, or a new type of heavy lepton like a massive electron or muon. Some theories require both neutral currents and heavy leptons. Groups at CERN and at the National Accelerator Laboratory at Batavia, Illinois, are looking for heavy leptons but no firm claims have yet been made, though a Harvard group at NAL, led by Rubbia, has also reported evidence for neutral currents.

So far only a fraction of the film from Gargamelle has been analysed. But to understand the neutral currents more thoroughly it will be necessary to study them in neutrino interactions on hydrogen, as well as collecting more of the events on heavy nuclei from the present Gargamelle experiment. One of the most readily available devices for studying neutrino-hydrogen interactions is Gargamelle herself, but with a propane filling (C_3H_8) instead of freon (CF_3Br). Gargamelle is better than a pure hydrogen chamber for this work because the propane is a denser liquid, which will detect many of the neutrons and gamma rays in the final state. Because there is pressure at CERN to close down Gargamelle before the propane experiment can take place, to save money for the new accelerator, a brisk debate is in prospect. The supporters of Gargamelle are not expected to go to the same lengths in defending their case as did their sixteenth century predecessors.

D. M.

Thermoluminescent Dating

THE various phenomena of luminescence provide useful diagnostic tools for the study of electron states in solids. Among them is thermoluminescence, which has been applied since the late 1940s to the dating of geological minerals and more recently to the dating of archaeological specimens, particularly by M. J. Aitken and his team in Oxford. The same phenomenon is now in common use for dosage measurements in radiology.

Many non-metallic solids are at least feebly luminescent and of these many show the thermoluminescence effect, that is, emission of luminescence on warming in the dark after suitable excitation at ordinary or lower temperatures. In the case of minerals and archaeological samples the excitation is the result of the cumulative effects of exposure to radioactive inclusions in the material or at the original site. In the simplest cases, therefore, warming of such samples in the dark in the laboratory can give a light emission which can be a measure of the total dose of excitation and so, if the excitation is a steady process over the years, an indication of the sample age. By laboratory calibration with standard radioactive sources the time scale can be established.

The most elementary mechanism for the thermoluminescence effect is that which assumes excitation to put electrons into metastable states or electron traps from

which they escape by a thermal activation process having a probability dependent on a Boltzmann type function $C \exp(-E/kT)$ where C is a constant, E another constant known as the trap depth, k Boltzmann's constant and T the absolute temperature. Such a function gives a very critical temperature dependence; for example, if for a given value of C traps of depth 0.1 eV hold electrons for a mean time of 2×10^3 s, then traps of depth 2 eV give mean lifetimes of 10^{18} s. Thus deep traps in solids form electron storage sites effective for geological times. The simple model is, however, not realistic as Wintle has shown on page 141 of this issue of *Nature*. Electrons leak away from traps at ordinary temperatures on account of what are effectively non-thermal processes. Such effects have been known for a long time in inorganic solids and the transition of electrons from triplet, metastable states in organic molecules to the singlet ground states by

direct but forbidden processes is also well known. In 1950 Garlick and Bull (*Proc. phys. Soc. Lond.*, **63**, 1283) reported a non-thermal phosphorescence decay involving loss of trapped electrons in diamond and having a lifetime of 10^5 s. Much later, similar effects in terrestrial labradorite and in lunar soil samples were described (Garlick and Robinson in *The Moon* (edit. by Runcorn, S. K., and Urey, H.), 324 (IAU, 1972).

There is no doubt that the existence of the anomalous loss of trapped electrons from storage sites in minerals and in other samples raises doubts as to the usefulness of the thermoluminescence dating methods. The effect can, however, be a minor one in many samples and the important procedure for anybody wanting to use the technique is to determine the degree of anomalous fading. This can be done, as in the work of Wintle, by studying the room temperature decay of the stored energy over sufficient time periods. It is also wise to take only that part of the thermoluminescence curve, namely the high temperature section, which arises from the release of electrons from relatively deep traps. There always remains the problem that tests for anomalous fading are limited in time scale to weeks or months for practical reasons and so low rates of loss must then be extrapolated to thousands of years or more. High accuracy of correction of dating curves is thus not possible.

It is fitting to add some explanation of the anomalous fading effects in minerals and archaeological specimens. It is now well known in luminescent and semiconducting solids that electron traps and luminescence emission centres are not remote from each other and that direct tunnelling of trapped electrons into centres can occur even at very low temperatures. Such quantum mechanical effects depend strongly on trap-centre separations and on the extent of overlap of wavefunctions for trapping and centre states; the last depend, for example, on trap depth and so for a typical mineral sample, or say pottery sherd, for which a wide distribution of trap depths occur there is a whole range of mean lifetimes for the anomalous leak process for trapped electrons. Thus no simple decay law emerges and in fact it is not surprising that the curve of Fig. 3 of Wintle's communication does not follow a simple exponential form. In the work of my team the common form is that of a power law process, produced by summation of many exponential decays. If Wintle's data of Fig. 3 are replotted on a log-log plot, a sensibly straight line graph results. This indicates, as expected, a wide range of trap depth distributions.

It is also worth pointing out that both in radiological dosimetry, using such thermoluminescent systems as lithium fluoride, and in mineral and archaeological specimen investigations there are other effects which can obscure the stored energy information. One of these is the introduction of surface states on samples by adsorption (of ambient water vapour, for example). Such states can provide leak paths for trapped electrons or even introduce spurious thermoluminescence effects. In most cases handling and operation in dry nitrogen seem to be effective in controlling or eliminating the unwanted disturbances. It must also be admitted that grinding up of samples before thermoluminescence experiments could be an important source of disturbance of electronic states and of new surface states; most experienced workers make control experiments to determine the extent of such effects in every type of sample they investigate.

G. F. J. G.

Aged Sediments

RECENT discoveries have pushed back the radiometric ages of early crustal rocks to the extent that probable ages of at least 3,800 m.y. are now widely accepted. These great ages are normally derived from analysis of such rocks as granites and granite-gneisses. Moorbath, O'Nions and Pankhurst now report on page 138 of this issue of *Nature* results of analyses of supracrustal rocks, including banded ironstones, from the Isua area of West Greenland near Godthaab; they deduce a probable age of $3,760 \pm 70$ m.y. The geological setting presents familiar problems in these Archaean terrains, because the metasediments occur in a (refolded) syncline among granitic gneisses, and the interpretation of the contact is difficult because of intense deformation; however, the two groups show similar metamorphic grade.

The gneisses yield a whole rock Rb-Sr isochron age of $3,700 \pm 140$ m.y. The banded ironstones have provided Pb-Pb isochron ages of $3,760 \pm 70$ m.y.—a remarkable application of this technique to such ancient sediments—and there is evidence of severe uranium depletion at or before this time. These ages are concordant, and the authors discuss the problems arising in a useful manner. Although these are the greatest ages yet reported for water-laid sediments, the "country" gneisses of the Godthaabsfjord area enclose rafts and enclaves of earlier rocks, which include what may well be metasediments of still greater age. The Isua metasediments are therefore at present to be regarded as the oldest to be dated, and their depositional age may well be greater, because the figure of $\sim 3,700$ m.y. may well represent a subsequent metamorphic event. It is clear that this early Precambrian cratonic area of the central belt of Greenland deserves still further study to elucidate the time sequence, structural details and sedimentary emplacement among the Archaean rocks.

In addition to these interesting results, the communication also brings out some outstanding new applications of Pb-Pb isochron work.

T. S. W.

Predicting Earthquakes

FOR some years now a body of evidence has been growing that there may be some premonitory symptoms of the occurrence of earthquakes. Of course, in a restricted sense one can predict earthquakes by looking at a world map of seismicity, drawing one's finger over all the seismic belts of the world and saying "it has happened there in the past and it will happen there again, because it is in the nature of plate boundaries to continue to manifest themselves by earthquakes". This is not a very useful approach because although undoubtedly very sound in the long term it imparts no immediacy to the problem of preventing people being killed by earthquakes. And immediacy seems to be the only concern of most people: residents of San Francisco and Los Angeles seem relatively unmoved by the prospect that there will be a major earthquake in the next fifty years.

One of the problems of predicting quakes in the past, however, has been a gloomy yet perfectly justifiable feeling that they may just happen when strains exceed a certain (unknown) value and that there simply is no prior revelation. This still may be true of very many earthquakes, and yet those who wanted to predict were encouraged by the signs that some earthquakes could be controlled, essentially by lubricating fault surfaces. This meant that some earthquakes, at least, were sitting and waiting for the go-ahead and the message came from fluids in the vicinity of the fault. And yet no amount of sitting and thinking about the problem would have revealed that there was an observable chain of events before some earthquakes occurred. This needed observations which were, in a sense, random. They were certainly not directed specifically towards monitoring the fault surface itself which would have been the most obvious thing to do and certainly prohibitively expensive.

In the late 1960s it became clear that some results of importance were coming from Russian experiments in the Garm area of the Soviet Union. Many physical properties in an earthquake region were being monitored on a regular basis, such as random emissions, electrical resistivity, water levels in wells, magnetic field variations and seismic velocities. Before earthquakes these properties would behave in an unusual way. Seismic velocity is a good example. Days before an earthquake it would appear that the ratio of velocities of compressional and shear waves would drop quite steadily to a value at least 20% less than its unperturbed value. Just before the earthquake the value would return to normal. Russian science is clearly motivated in ways different from Western science, for this singular result which, if discovered in the United States, would have been published within months and advertised in every possible way, lay fallow for a long time—indeed much of the credit that earthquake prediction has advanced so far in the past year or two belongs to the indefatigable Professor Lynn Sykes (Lamont-Doherty Observatory) who went to Garm to find out what was going on.

From then on the inexorable Lamont machine started rolling, and, as it has done several times in the past, did not take long to get answers. They came from, of all places, upstate New York where Lamont had deployed some instrumentation to study small earthquakes. It transpired that here too velocity ratio changes of up to 20% were being observed, and these effects were spread

throughout a region considerably larger than the roughly planar surface of the fault.

Suddenly travel times in focal regions became all the rage and an important additional observation was made by Whitcomb, Garmany and Anderson, of California Institute of Technology, that P-wave velocities in the vicinity of the San Fernando earthquake of 1971 seemed to have been perturbed for several years before the quake.

It became apparent at this stage that the velocity anomalies and indeed other anomalies too were understandable if dilatancy was behind it all. (A report by Scholz, Sykes and Aggarwal (*Science*, **181**, 803; 1973) has recently packaged observational data and the makings of a physical theory rather neatly.) A water-saturated rock under increasing strain may reach a stage where the opening of new cracks cannot be matched by the flow of fluid into these cracks. The "pore pressure" thus drops and so does the compressional wave velocity. This process, however, leads eventually to the rock being hardened and at this stage no more cracks form, but the water continues to flow into the unsaturated region. This now increasing pore pressure (with compressional velocity returning to normal) leads finally to an earthquake by the same process as do the earthquake control experiments mentioned previously. Thus, a train of events is set in motion some time before the earthquake occurs which inexorably leads to rupture, and furthermore the changes in physical parameters are sufficiently gross to be observed in the general region of the earthquake. Another attractive feature of this notion is that because the size of the dilated region will be related to the size of the fault length (and thus approximately to the magnitude of the earthquake) and also the duration of the above-mentioned processes will be controlled by diffusion processes in the dilated region, there should be a relation between the time duration of the precursor and the size of the earthquake. Quite remarkably, this seems to be working out well—Scholz *et al.* and Whitcomb *et al.* have found an approximate relation over three orders of magnitude in precursor time between the latter and the square root of the length of the ruptured zone.

Not all earthquakes appear to show these effects, and the boast of Scholz *et al.* that "earthquake prediction . . . appears to be on the verge of practical reality" is no more than an enthusiastic opinion; nevertheless, an enormous research field has opened up. Up to the present many seismologists have been dubious of the data because of the great difficulty of reading seismograms (particularly shear wave arrivals) to the required accuracy. A communication in this issue of *Nature* (see page 139) may go some way to dispelling these worries, as the readings were made not by participants in the frenzied activity of the past year but by Japanese technicians ten years ago.

Wyss and Holcomb examined the possibility that seismic stations sitting in the vicinity of potential earthquakes can see this velocity anomaly using compressional waves that have travelled nearly vertically through the dilated region from distant and entirely unrelated earthquakes. One of the problems with work previously reported has been that sources of seismic waves have necessarily had to be small earthquakes in the focal zone, with the obvious disadvantage that it is more difficult to use standard seismic velocities to locate these quakes accurately than to use the accurate location but infer anomalous seismic velocities. Although this objection has been well known to Scholz *et al.* and Whitcomb *et al.*, and they have done

their best to obviate it, the work of Wyss and Holcomb is a great encouragement. The authors studied the station Matsushiro in Japan before and after a large swarm of events in 1965. They simply used times of arrival of waves reported by the station operator and compared them with expected arrival times. A large body of data is used and it is clear from their Figure 1 that the so-called residual is time varying. The time duration of the normal and its amplitude both fit in well with expectations from other information operators of the swarm; thus in hindsight an event could have been predicted.

This is a remarkable result which shows among other things that there are still good things in existing geophysical data for those who can look for them with a new eye.

D. D.

Sequencing the Messenger

RECENT advances in sequencing RNA molecules have been at once stimulating and frustrating. Direct comparison of the nucleotide and amino acid sequences has, of course, been a new and powerful probe to demonstrate the meaning of the genetic code. But one of the most intriguing aspects of the RNA sequences at present identified is the existence of quite long stretches of untranslated polynucleotide chain at the beginning and end of, and between, the genes. Because the only RNA molecules which could be obtained in sufficient quantities to analyse were those of the RNA phages, the implications of this discovery are not unambiguous.

The RNA phage both serves as a template for protein synthesis by the ribosomes and must also be packaged into the limited space of the phage particle, so that the extensive features of secondary structure found in its 3,500 nucleotides might be the response to the evolutionary demands of either situation. That the sequences additional to the genes themselves and their features of secondary structure are not the consequence of some demand of the translational apparatus is suggested by the absence of any noted homologies between the various initiation and termination regions of the genes of the phages of the f2 and Q β group. But the discovery of untranslated sequences and of appreciable secondary structure in an RNA which serves as a messenger at least suggests that such parameters may be implicated in its translation. To confirm or deny such concepts requires, of course, the characterization of some messenger of *Escherichia coli* which serves only the function of coding for protein. The beginning of just such an experimental analysis is reported in the current issue of the *Proceedings of the National Academy of Sciences* by Bronson, Squires and Yanofsky (70, 2335; 1973) in an extension of the work of Yanofsky and his colleagues on the tryptophan operon of *E. coli*.

One considerable advantage offered to researchers on the tryptophan operon is the large number of bacterial strains which have been isolated with deletions of parts of it and the derivation from them of phage molecules of $\phi 80$ which carry particular regions of this operon. Squires *et al.* were therefore able to isolate the RNA of the beginning of the tryptophan operon by hybridizing RNA synthesized by one deletion strain of *E. coli* with the DNA of a phage $\phi 80trp$ molecule carrying only the *trpE* gene (which thus provides the only homology between

the *trp* mRNA of the bacterium and that of the phage). By obtaining T1 ribonuclease fingerprints of the hybridizing RNA, they were able to show that their complexity increases as the RNA is derived from a series of strains which possess increasing lengths of the start of the *trpE* gene. The oligonucleotides found in deletion strains can therefore be assigned to different groups by their presence or absence in each strain, giving some indication of which part of the beginning of the *trpE* gene they represent.

From the sequences of some of these oligonucleotides, Squires *et al.* deduced a stretch of forty-three bases which corresponds to the first eleven amino acids of the polypeptide specified by the *trpE* gene. Confirmation of the identity of the nucleotide and protein sequences was elegantly provided by the demonstration that the messenger sequence represented by these oligonucleotides is altered by genetic mutants in the starting region of the *trpE* gene. The absence of these particular nucleotide sequences in two deletion strains with the least part of the *trpE* gene (identified as such by genetic analysis) indicates that the sequence coding for the start of the protein does not lie at the 5' end (the starting region) of the messenger. It must therefore be preceded by a nucleotide sequence which is either untranslated, or which, if translated, specifies some small polypeptide the existence of which has previously been quite unsuspected.

The example of the RNA phages argues that the sequence on RNA representing the *trpE* gene is most probably preceded by a sequence of RNA which is not translated. In the RNA phages, this sequence extends for an appreciable distance, of the order of 200 nucleotides. How great is this distance in the *trp* messenger? The total length of nucleotides present in the strains possessing most of the beginning of the *trpE* gene and absent from the deletion possessing only the initiation sequence of its protein is of this same order of size—the untranslated sequence must be at least 150 nucleotides long.

Most of the functions which have been attributed to the "leader" sequence of the phage RNAs are inapplicable to a bacterial messenger, which does not need to be compressed into a phage particle and which does not recognize an RNA replicase to catalyse its reproduction. That this sequence may have some regulatory role in the tryptophan operon is suggested by the previous observation of Jackson and Yanofsky (*J. molec. Biol.*, 76, 89; 1973) that the deletion mutants lacking this part of the operon synthesize increased amounts of the tryptophan messenger. Some mechanism which acts on this region thus seems to achieve a repression of the operon which is independent of the usual repression mediated by the interaction of repressor and operator. In an intriguing preliminary report of attempts to sequence the beginning of the tryptophan operon messenger, Cohen, Yaniv and Yanofsky (*J. molec. Biol.*, 74, 163; 1973) observed that distinct and reproducible bands are produced on gel electrophoresis of its mRNA. They suggested that these bands might be the result of cleavage *in vivo* of the RNA at a small number of specific points. Whether this cleavage might be related to the regulatory mechanism which seems to act in this region is, of course, at present a matter for speculation.

Although originally hailed as the beginning of a detailed analysis of messengers which would throw new light on the controls and interactions of transcription and translation, the sequencing of RNA phages has recently come to be regarded as an interesting and important contribution

to molecular biology, but one nevertheless which fails to say much about the mechanisms of nucleic acid metabolism in the uninfected bacterial cell. The tantalizing hint thrown up by the report of Squires *et al.* is that the parallels between phage RNA and messenger RNA may after all show the type of relationship originally attributed to them. If bacterial messengers prove to have the same class of secondary structure and untranslated sequences which prevail in the phages, mechanisms now only dimly suspected may prove to be of critical importance in gene expression.

From our Molecular Genetics
Correspondent

SPINA BIFIDA

Stopping a Second Strike

from a Correspondent

It is distressing for any family to have a child with hydrocephalus or spina bifida—to produce further children with similar defects is a tragedy, yet the likelihood of doing so is variously estimated at 1 in 5 or 10.

Efforts are being made to diagnose the affected foetus so that the parents may be offered termination of that pregnancy. Ultrasound may detect enlargement of the foetal head, and X ray may show an abnormally large head and defects of the spine, but some affected fetuses may remain undetected by both these methods until the pregnancy has proceeded too far for an abortion to be carried out safely. It now seems that the measurement of α -foetoprotein in the amniotic fluid may be the solution to this problem.

A retrospective study published last year suggested an association between α -foetoprotein and congenital abnormalities of the central nervous system. The technique involves obtaining samples of the fluid surrounding the foetus by amniocentesis—introducing a needle through the mother's abdominal wall and uterus into the amniotic sac. This technique is not without hazards. It may possibly induce abortion by irritation of the uterus, or haemorrhage by piercing the placenta, but it is already widely practised for the detection of other disorders such as rhesus haemolytic disease. Technically amniocentesis is not difficult to perform after 10 to 12 weeks, but before this difficulties arise due to the small volume of fluid present.

Now the results of a prospective study have been published (Allan *et al.*, *Lancet*, ii, 522; 1973). It is based on 120 samples of amniotic fluid, mostly collected for other investigations, such as the detection of haemolytic disease

or chromosome abnormalities, but some coming from twenty patients with a history of at least one previous pregnancy involving a gross abnormality of the central nervous system.

The results show a good correlation between high α -foetoprotein levels and affected fetuses, particularly for samples taken between 12 and 20 weeks' gestation. This is the time when amniocentesis is most conveniently performed, and is still sufficiently early for a foetus to be aborted if necessary.

Very high α -foetoprotein levels were found in seven of nine samples from pregnancies in which the foetus turned out to have a gross neural tube defect—the two apparently normal samples from this group were taken at 6 and 39 weeks' gestation so do not detract from the significance of the results since these are outside the normal limits for amniocentesis. Two of the seven samples were from patients with a history of nervous system abnormalities in previous pregnancies. These two patients accepted termination, and the fetuses had abnormalities of the central nervous system.

So of the twenty patients particularly at risk because of their history, two have already had terminations. The remaining eighteen had normal α -foetoprotein levels and six have already delivered normal infants. Unfortunately the work was published before the outcome

of the other twelve pregnancies was known, but it already looks as if this method is going to be the best way of spotting recurring cases of neural tube defects.

PALAEOZOOLOGY

Ancestry of Chordates

from a Correspondent

ONE of the most controversial questions to have taxed the minds of zoologists is to which of the great invertebrate groups are the vertebrates most closely related. Few people would argue today that the echinoderms fill this role. The evidence for this view is largely embryological: both groups are deuterostomes (those bilaterally symmetrical animals in which the embryonic blastopore becomes the anus). What is still a matter of debate, however, are the relations of two smaller groups of living deuterostomes—the urochordates (sea squirts) and cephalochordates (*Amphioxus*)—to one another, and to the echinoderms and vertebrates. The view currently accepted places *Amphioxus*, derived by neoteny from the tadpole larva of urochordates, close to the origin of the vertebrates.

Jefferies (*Phil. Trans. R. Soc.*, 265, 409; 1973), in drawing attention to the recent findings of other workers, now removes *Amphioxus* from this position.

B-cell Mitogens *in vitro* do not Require Complement

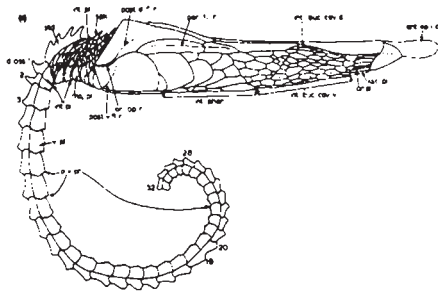
BIOLOGICAL scientists, attempting to wrest order from the materials of their investigations, often adopt unifying hypotheses. With almost the same high frequency, such attempts at formulation of rules are found to have exceptions, often so numerous as to invalidate the original generalization. An instance of such reappraisal emerges from the communication of Janossy *et al.* in *Nature New Biology* for September 26.

Janossy and his colleagues used various preparations of bacterial lipopolysaccharides (LPS) to stimulate the lymphocyte populations in mouse spleen *in vitro*, and conclude, first, that various LPS populations have mitogenic activity; second, that the response is predominantly of B lymphocytes (that is, those cells not derived from the thymus); and, third, that the response is polyclonal and not equivalent to the "clonal" responses to specific antigens. They note that although their various LPS preparations differed in their capacity to activate complement there was no correlation between this property and mitogenicity. On this basis their first thought was that complement, and in particular C3 activation, is not necessary for B-cell mitogenicity in these conditions.

Janossy *et al.* then undertook a series of experiments designed rigorously to

remove or destroy the C3 component of complement in their cultures. However hard they tried they were unable by the various exclusion methods to demonstrate significant diminution of the response of B cells to LPS. They conclude that their results provide no support for the notion that C3 activation is a prerequisite for the direct triggering of B cells by LPS (or pokeweed mitogen). This interpretation is in line with other studies which have shown that agents which destroy C3 reduce or suppress T (thymus-derived) cell dependent immune responses but do not affect T independent responses. Other workers, however, have proposed, partly on the basis of the demonstration of C3 receptors on B cells, that C3 is important in the non-specific stimulation of B cells.

It seems that although the importance of C3 in the cooperative activities of B cells with T cells is likely, the direct stimulation of B cells does not involve complement. Furthermore, it is probably coincidental that some B-cell mitogens can activate the alternate complement pathway (by way of C3). Janossy *et al.* maintain that it is the efficient multipoint cross-linking of surface receptors by polymeric ligands which determine B-cell mitogenicity *in vitro*.



Jefferies's restoration of *Lagynocystis*, an ancestor of *Amphioxus*? (from *Phil. Trans. R. Soc.*, 265; 1973).

The urochordate tadpole and vertebrates share specializations — for example, motor endplates — which *Amphioxus* does not. Jefferies reports that he has found fossil evidence for his view in a hitherto obscure group, previously held to be primitive echinoderms. These, which he has renamed the calcichordates, he has resurrected (in a series of papers) with spectacular success. He considers one group of calcichordates, the mitrates, to be the common ancestors of *Amphioxus* on the one hand, and of the urochordates and vertebrates on the other. The common specializations which Jefferies believes are shared by a group of swimming mitrates and vertebrates are: "a brain, a complex nervous system and a body clearly separate from the tail". *Amphioxus* on the other hand he considers to be descended from *Lagynocystis*, a burrowing mitrate, which he describes in this new paper.

It must be said, however, that many of Jefferies's colleagues find it difficult to accept such a radical reassessment of the phylogeny of *Amphioxus*. In trying to convince them Jefferies is up against the perennial problem faced by palaeontologists when describing groups, such as the calcichordates, which are very different from any living today. There is no way of knowing whether the soft parts have been accurately identified; this being the case it is difficult to see how hypotheses concerning the evolutionary relationships of such animals can be tested.

ECOLOGICAL GENETICS

Genic Heterozygosity

from a Correspondent

Selander and Kaufman in a recent paper (*Proc. natn. Acad. Sci., U.S.A.*, 70, 1875; 1973) use data from their own and other electrophoretic studies to show that populations of invertebrates have higher levels of heterozygosity than do those of vertebrates. In the invertebrates studied, polymorphisms occur at a higher proportion of loci and, on average, more alleles are segregating at each polymorphic locus than in the vertebrates. By suggesting that these differences reflect different ways in

which populations of small and large organisms experience their environments, the authors "take sides" in two independent controversies.

First, to account for allozymic variation in adaptive terms implies non-acceptance of the view expressed by several mathematical geneticists that observed levels of heterozygosity are too high to be maintained by natural selection, and that most of the electrophoretic variants must be of neutral survival value relative to each other.

Second, in order to predict differences in the mode of action of selection on vertebrates and invertebrates, Selander and Kaufman use Levins's conclusion (*Evolution in Changing Environments*, Princeton University Press, 1968) that polymorphism is the response of a population to a spatially or temporally unpredictable environment. For example, where a population exists in a spatially variable environment, each individual may either spend most of its life in one type of "patch" or may cover most of the different types in the proportion in which they occur. In the first case, which Selander and Kaufman argue is general for invertebrates, including larvae of flying insects, because of their small size, low mobility and limited potential for homeostatic control, different individuals in the population are exposed to different environments. In the second, supposedly more characteristic of vertebrates, each individual must

survive in all environments. Levins's conclusion that the first type of selection leads to polymorphism whereas the second tends to give a single all-purpose genotype sounds logical, but has been criticized by Hamilton (*Science, N.Y.*, 167, 1478; 1970) who found that it was based on unrealistic population dynamic assumptions.

Although Levins has shown that polymorphism is the optimum population strategy in an unpredictable environment, the classical view has been that disruptive selection, that is, selection acting in more than one direction simultaneously does not give rise to polymorphism unless the selective advantage of an allele is dependent on its frequency, such that individuals with rare alleles are favoured. Thus, it seems that the degree to which Levins's conclusions apply must depend in part on the balance between selection pressures acting at the population and individual levels. This question itself is complex and controversial, the outcome being much dependent on the population structure of the species concerned.

For these reasons it seems that, if the term "neo-Darwinist" is to lose its aura of condescension, the "neutralists" must be attacked in other ways. This can be done by basing predictions of the action of natural selection on specific metabolic functions of the enzymes concerned, or by detailed ecological and

Isolation of H Chain mRNA Precursor

Stevens and Williamson have previously reported that myeloma cell heavy (H) chain mRNA binds to the total protein H_2L_2 and that, after precipitating with antiserum to H_2L_2 , the RNA can be recovered. Using this method three different RNAs have been isolated; two were found in both nucleus and cytoplasm, but the largest only in the nucleus. The two smaller RNAs were shown to direct the synthesis of H chain when injected into *Xenopus laevis* oocytes and in *Nature New Biology* next Wednesday (September 26) Stevens and Williamson describe a technique which allows the largest RNA to be isolated in sufficient quantity for injection into oocytes. Increasing the concentration at which the cells are grown from 5.7×10^6 to 10^7 cells ml^{-1} results in an accumulation of nuclear RNA until 80% of the RNA isolated by binding it to H_2L_2 is nuclear in origin. After separating the three RNAs on polyacrylamide gels the largest can be eluted for injection into oocytes. This results in the production of myeloma H chains.

Because the largest RNA contains the sequence of nucleotides which codes for H chain and is confined to the nucleus, it seems likely to be the precursor of

cytoplasmic H chain mRNA. To prove this the authors performed pulse-chase experiments and were able to show that the largest RNA is synthesized before, and gives rise to, the smaller RNAs. The cleavage takes place in the nucleus — the whole procedure being analogous to the production of ribosomal RNA. The two RNAs (which appear in both the nucleus and cytoplasm), although apparently very different in molecular weight (6×10^5 and 3.1×10^5), are not thought to represent different stages in the processing of mRNA. Their true molecular weights are probably much closer — the large difference arising from different electrophoretic mobilities depending on whether or not they contain poly(A)-rich sequences.

Previous attempts to demonstrate a precursor-product relationship between high-molecular-weight nuclear RNA and cytoplasmic mRNA have not been completely successful because of the difficulty of working with both easily labelled and uniquely identifiable RNA molecules. Stevens and Williamson have met this difficulty by using differentiated cells which grow in culture with the result that the precursor-product relationship is most successfully demonstrated.

genetic comparisons of closely-related species or populations of a single species. Differences between vertebrates and invertebrates are too many and too intangible to be valuable in this type of comparison.

VAN DER WAALS

Honoured Again

from our Statistical Mechanics Correspondent

VAN DER WAALS'S OWN university of Amsterdam celebrated the centenary of the publication of the famous equation by organizing a conference on statistical mechanics (under the auspices of the International Union of Pure and Applied Physics) which took place between August 26 and 31. It was on altogether a larger scale than the Centenary Conference held at the University of Kent in April (see *Nature*, 243, 263; 1973), the programme of which was practically confined to liquids and critical phenomena.

The main emphasis of the conference was on the fields opened up by van der Waals—the equation of state, corresponding states and scaling laws, mixtures and surface tension. It was possible to hear all the invited papers (if not all the contributed ones), which should retain their interest as surveys for many years to come. One was continuously reminded that science almost never advances in the clean and tidy way that might be imagined from a superficial reading of its history.

For example, J. de Boer (University of Amsterdam) and M. J. Klein (Yale University) showed what a gross error it would be to say that van der Waals simply used some then current ideas to give a nice interpretation of the work of Andrews. In fact, van der Waals's real roots go back to Laplace and Newton. J. M. H. Levelt-Sengers (US National Bureau of Standards) recalled that discrepancies between experiment and the van der Waals critical exponents were known in 1900, but had to wait until 1965 for a satisfactory interpretation. Scaling laws and their possible origins were discussed by B. Widom and K. G. Wilson (both of Cornell University). J. L. Lebowitz (Yeshiva University) showed that the equilibrium van der Waals equation can now be rigorously derived, but that serious doubts remain about the metastable regions of the van der Waals loop, which were also discussed by J. S. Langer (Carnegie-Mellon University).

Difficulties become even more severe when attempting to discuss apparently simple transport phenomena in a fluid, as was shown by P. M. Résibois (Free University, Brussels) and by B. J. Alder (University of California, Livermore). R. B. Griffiths (Carnegie-Mellon Univer-

sity) discussed the new phenomenon of a "tricritical point" that occurs with mixtures, E. M. P. Guyon (University of Paris, Orsay) described instabilities in liquid crystals and E. B. Smith (University of Oxford) surveyed present knowledge of intermolecular potentials, the raw material of theory. Exactly soluble models of phase transitions were reviewed by E. H. Lieb (Massachusetts Institute of Technology) and melting, obviously a much more complicated phenomenon than evaporation, was dealt with by H. Mori (Kyushu University); this last contribution provoked a lively, but quite friendly, discussion. J. van Kranendonk (University of Toronto) showed what detailed information is now available from spectroscopy about mechanisms of collision, induced dipole moments and the formation of bound complexes.

A sad note was struck by the contribution on specific heats by A. V. Voronel (USSR) (read in his absence by C. Domb) which called attention to the difficulties caused by gravity (not fully appreciated until the 1950s), the necessity for stirring and surprisingly that, from the point of view of deriving critical exponents from experimental results, it can matter very much which of several possible alternatives one chooses as the definition of the "order parameter".

OPHIOLITES

Troodos as Arc Volcano

from our Geomagnetism Correspondent

THE search for evidence to support the idea that the Troodos Massif of Cyprus is an upthrust fragment of ancient ocean floor has been going on for more than a decade. During this period there have been several individual disappointments and setbacks, although the chief problem has been not so much the unwelcome discovery of evidence conflicting with the ocean floor hypothesis but the inability to obtain data giving unequivocal support. As a result, the hypothesis has had few, if any, active opponents, and most people with an interest in the situation have been content either to suspend judgment or to accept the circumstantial evidence.

But this happy consensus has now been broken by Miyashiro (*Earth planet. Sci. Lett.*, 19, 218; 1973), who argues against one of the basic concepts involved. The Troodos Massif is, of course, an ophiolite complex; and in recent years it has come to be accepted, at least by supporters of plate tectonics, that ophiolite complexes were formed at oceanic ridges. Miyashiro, however, has carried out an analysis which, he claims, shows that the Troodos rocks are chemi-

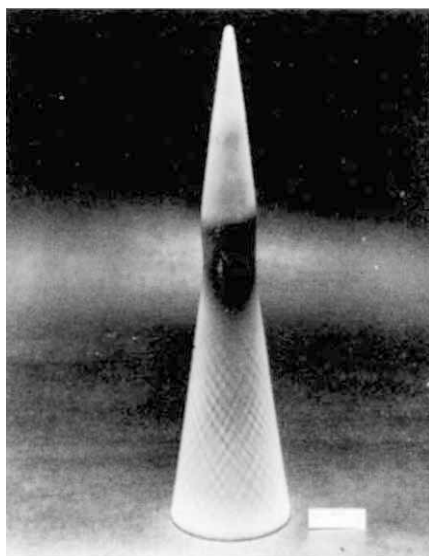
Turbulent Gas Flows on the Moon

THE idea that surface markings on some parts of the Moon were produced by supersonic turbulent gas flows is re-examined in next Monday's *Nature Physical Science* (September 24) by Rehfuess and Larson. It has been previously thought that these lineations were produced by outgassing; recent work by Rehfuess, however, pointed to

an association with gas produced in vaporization during meteor impacts (*J. geophys. Res.*, 77, 6303; 1973). The second possibility now seems to be supported by a pattern of cross-hatching found at Silver Spur, a feature near the Apollo 15 landing site.

Diamond shaped patterns, or cross-hatching, are a common feature of wind tunnel ablation studies (see figure) and are also found on recovered flight vehicles. Such patterns also occur on the Moon, notably where two sets of lineaments intersect about 20 km south of the Apollo 15 landing site, suggesting strongly that the area has experienced supersonic turbulent flow. Such a flow can be produced in the expanding gas cloud which forms when a meteorite strikes the Moon at a speed above 16 km s⁻¹, regardless of the size of the meteorite.

Clearly, if the model is correct then there should be a young crater near to the Silver Spur cross-hatching. Rehfuess and Larson discuss the plausibility of the candidature of several nearby craters, and suggest that the best possibilities are Aristillus, Autolycus and Aratus. If any of these three craters was produced by a meteorite impacting at sufficiently high speed the impact could have produced the required turbulent flow at Silver Spur.



Cross-hatching ablation pattern on teflon surface produced during tests at Marshall Space Flight Center.

cally distinct from those produced at oceanic ridges and more closely resemble the volcanic piles in immature island arcs with relatively thin oceanic-type crust. In other words, he proposes that the Troodos Massif was created as a volcano in an island arc between Eurasia and Africa.

The chemical basis of Miyashiro's analysis is the variations of the ratio FeO^*/MgO (an increase in which is a measure of the advances in fractional crystallization of basaltic magma) with FeO^* , SiO_2 and TiO_2 —variations which enable distinctions to be made between the tholeiitic series and the calc-alkalic series of igneous rocks. For example, when SiO_2 is plotted against FeO^*/MgO over the approximate FeO^*/MgO range 2–5, the rate of increase in the SiO_2 content as fractional crystallization progresses is found to be much lower for tholeiites than for calc-alkalic rocks, and a definite dividing line may be perceived between the low gradient tholeiitic rocks and the higher gradient calc-alkalic rocks. This distinction is even more convincingly demonstrated by the variations of FeO^* with FeO^*/MgO . As fractional crystallization proceeds in tholeiitic rocks the FeO^* content rises to a maximum and then decreases; in calc-alkalic rocks, by contrast, FeO^* decreases monotonically. A similar pattern is also observed for the variation of TiO_2 with FeO^*/MgO . Moreover, these trends are apparently altered very little by metamorphism or other secondary processes.

The relevance of these distinctions to the Troodos Massif is that certain of the Massif rock compositions fail to fall into the group expected on the basis of an origin at oceanic ridges. Most, if not all, non-alkalic igneous rocks from the deep ocean floor are known to be tholeiitic. Whether or not there are any calc-alkalic rocks of genuine ocean floor origin is still a moot point, but if there are, the results of dredging suggest they must be very rare. Plots of SiO_2 , FeO^* and TiO_2 against FeO^*/MgO for samples of the lower pillow lavas and the sheeted complex from the Troodos ophiolite sequence show, however, that a relatively high proportion follow the calc-alkalic trends described earlier. The data points are quite widely scattered; and there can be no doubt that many of them represent tholeiitic rocks as expected. But for about one-third of the samples, SiO_2 increases rapidly and FeO^* and TiO_2 decrease rapidly with increasing FeO^*/MgO in accordance with calc-alkalic behaviour.

The implication of the presence of such a high proportion of calc-alkalic rocks is that the Troodos Massif is unlikely to have been created at an oceanic ridge. Moreover, on the more positive side, a relative abundance of calc-alkalic rocks is more in keeping

with volcanism in island arcs and continental margins, as Miyashiro himself recently showed (*Am. J. Sci.*, **272**, 629; 1972). And to make his case even stronger, Miyashiro points to a possible modern analogue of Troodos. Hachijo-jima is a small volcanic island in the northern Izu-Bonin Arc; and the FeO^* , SiO_2 and TiO_2 plots for its rock compositions bear a remarkable resemblance to the corresponding Troodos plots. The chief difference is a smaller proportion of calc-alkalic rocks on the island. In other words, in Hachijo-jima there is a volcano, demonstrably produced in an island arc environment, yet having a less developed calc-alkalic series than in a supposed segment of old oceanic floor where the occurrence of calc-alkalic rocks is theoretically unlikely.

But what of other geochemical work that has been taken to support the concept of Troodos as oceanic crust? Kay (*Eos*, **53**, 536; 1972), for example, claimed that the rare earth element abundance patterns from Troodos igneous rocks resemble those from abyssal tholeiites. Miyashiro's reply to this, quoting Schilling (*Phil. Trans. R.*

Soc., **A268**, 663; 1971) as authority, is that the patterns from island arc tholeiites also resemble those from abyssal tholeiites—and so Kay's data are also consistent with the concept of Troodos as island arc volcano. A similar consistency is claimed for the Ti, Zr and Y abundances reported by Pearce and Cann (*Earth planet. Sci. Lett.*, **12**, 339; 1971).

Finally, as Miyashiro recognizes, one of the arguments in favour of Troodos being oceanic crust is the presence of dyke swarms (sheeted complex), interpreted as representing oceanic ridge-type crust formation. This does pose a problem in that on island arc volcanoes such as Hachijo-jima no parallel dyke swarms are observed on the surface. The deep structure of island arc volcanoes is, however, little known; and so dyke swarms may exist at depth. Moreover, a dyke swarm does not seem to be a necessary component of ophiolite complex. The Vourinos complex in northern Greece has both tholeiitic and calc-alkalic trends (again suggesting island arc formation) but no marked dyke swarm.

Benioff Slopes and Mineral Deposits

METALLOGENIC belts near both old and new consuming plate margins have been related to the underlying presence of Benioff zones. But although the models developed have incorporated Benioff zones which remain stationary or migrate oceanwards (to accommodate the production or extension of marginal basins), the zones have usually been regarded as having constant slopes. In *Nature Physical Science* next Monday (September 24), however, Mitchell argues that the slope of a Benioff zone is an important variable, governing not only marginal basin spreading and the migration of island arcs but also the nature of the deposits emplaced near continental margins.

As far as the tectonics is concerned, most island arcs overlying Benioff zones which dip at angles greater than about 35° are associated with late Cainozoic extension of the marginal basins or, more rarely, major displacement along strike-slip faults. Mitchell thus suggests that the development of marginal basins only occurs above Benioff zones with steep or moderate dip. The variation of dip from one Benioff zone to another is, however, not the only sense in which dip may be regarded as variable, for the dip of a single zone may vary with time. There is some evidence, for example, that the marginal basin spreading behind the Marianas arc is cyclic, spreading only occurring when the dip is steep, and that the changes in dip are related to changes in the rate of descent of the lithosphere.

Both between-zone and within-zone variations of dip are involved in Mitchell's more important thesis, which is that the type of metallogenic belt formed at any given time depends on whether the dip of the corresponding Benioff zone is shallow or steep. Arguing from particular examples, Mitchell concludes that deposits of tin, tungsten, bismuth and fluorite and associated granites are emplaced near continental margins only above shallow-dipping Benioff zones. Porphyry copper deposits, on the other hand, are emplaced in andesitic and tonalitic rocks on continental margins and island arcs above steeply dipping Benioff zones, although they may also occur in silicic volcanic rocks above tin-bearing granites associated with shallow-dipping zones. The occurrence of copper in both types of environment suggests, however, that it might be possible to recognize two gradational types of porphyry deposit—and there is already a little evidence for this. It seems, for example, that copper-molybdenum deposits are more frequently observed in association with silicic volcanic rocks (shallow dip) and that copper-gold deposits are more common in the andesitic environment (steep dip).

Finally, this work suggests the theoretical possibility that Benioff zone models might be used to aid mineral exploration. Mitchell warns, however, that interpreting the distribution of metallogenic belts is one thing but prediction is quite another.

Hope for the Technological Solution

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The pollution crisis forecast by a well publicized "world model" has been traced to a typographical error in the program. The corrected, slightly revised model shows growth being limited before the year 2100 if the appropriate technology is introduced before the year 2000. Affluence without restrictive social policies is apparently attainable.

THE use of computer simulation to study the problem of population and industrial growth on a world scale has been published by Forrester¹ and Meadows² under the auspices of the Club of Rome. Their models have generally forecast an "overshoot" mode for population, industrial output and food production which has been interpreted as human disaster involving billions of people before the year 2100. These workers were particularly pessimistic about the possibility of averting disaster through the use of conventional technological and economic approaches. Rather, they foresaw a need for social policies which have been seen by others^{3,4} as restrictive of freedom.

Forrester and the Meadows team have invited alternative formulations or policy approaches. The work reported here proceeded as follows. The original computer programs were obtained and translated into the Fortran computer language; validation runs were then made on a small scientific computer (IBM 1130) and alternative policies were tested. During the translation step using the Meadows model, a typographical error was noted in the original program listing—one number in a sequence was larger by a factor of 10 than its companions; this was corrected. During validation, major discrepancies were found between the results from the transplanted program and those originally published in three of the twelve runs reported. These were positively traced to the numerical error noted. The behaviour of the corrected version of the program was used to determine alternative policies. These policies lead to simulation results which show that, through the use of conventional technology and economics, the world can achieve a growth-limited situation corresponding to widespread affluence.

When the typographical error is corrected, and no other changes are made, the response of the Meadows model is as shown in Fig. 1. In this run, he has incorporated the following technological advances, effective in 1975: (1) World natural resources doubled over the "current best estimate"; (2) low cost energy supplies, which have made possible a reduction by a factor of four in resource consumption and pollution per unit of output; (3) agricultural technology which doubles the yield of land; (4) completely effective birth

control used by all—but actual family size is a matter of personal choice.

Corrections

According to the uncorrected Meadows model, a pollution crisis ensued in spite of the technological advances; a situation which does not occur⁵. (On page 139, with reference to Fig. 40, the authors say "Although a strict pollution control policy is still in effect, so that pollution per unit of output is reduced by a factor of four, industry grows so quickly that soon it is producing four times as much output." Not so, output goes up by only a factor of about two, not enough to trigger a pollution crisis. The reader can make a rough verification of this by comparing Fig. 36 and Fig. 40, using a straight edge to extrapolate industrial output per capita (population is similar in the two Figures) and a scale to estimate the relative magnitudes.) As Fig. 1 shows, the behaviour of the corrected model has the following favourable aspects: world population stabilizes below 6,000 million with low birth rate and long life expectancy; pollution is under control. The disturbing properties of the run are that food and industrial production have gone through overshoots and have fallen abruptly. On balance, the world in 2100 has seen better days than we have seen or it will see again.

Any version of the model which stabilizes population and controls pollution warrants further study. Apparently, the error noted earlier prevented the original workers from seeing

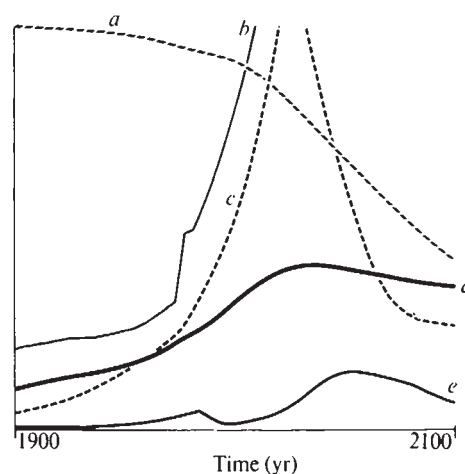


Fig. 1 Simulation results for the world model with extensive technological advances introduced in 1975. The curves go through standard world statistics for 1900 and 1970. Vertical scales have been omitted following the procedure of Meadows; scales are identical to those used by him. *a*, Resources; *b*, food per capita; *c*, industrial output per capita; *d*, population; *e*, pollution.

how close technology had come to achieving a satisfactory limit to growth. With the corrected run as a guide, it is contended that the technological policies are sound, but the economic policies in the simulation which control industry and agriculture are deficient.

A study of the agricultural section of the Meadows model reveals that the following aspects are simulated: (1) The favourable effect on land yield of capital-intensive farming; (2) the possibility of bringing uncultivated land under cultivation through the use of capital at a cost which increases as the supply of land decreases; (3) the allocation of capital between capital-intensive farming and new land development based on the marginal productivity of capital in each area; and (4) the irretrievable loss of soil fertility under over-intensive farming.

A study of the industrial section of the Meadows model reveals the following properties: (1) Industrial output is allocated to resource extraction, consumer goods, and capital for the food and service sectors; (2) all output not so consumed is reinvested in the industrial sector; and (3) consumption functions are used to settle the split of industrial output among the above categories—these show no decline in demand up to very high levels of consumption of food, services and goods.

Alternative policies which would tend to alleviate the problems remaining in Fig. 1 are as follows: (1) Modify the economics of the agricultural sector to discourage the use of capital-intensive farming above the level at which soil depletion becomes serious and divert the capital to land development instead; (2) simulate a moderation of demand for food and goods such that some of the excess industrial output is retired because of lack of good investment opportunities as productivity per capita reaches high levels. Figure 2 shows the results of a simulation run with the model modified to incorporate the above policies. This run has the following very favourable aspects: (1) Growth is halted in all sectors of the society; (2) the overshoot modes in food and industrial output have been avoided; (3) the stabilized population of less than six billion people is affluent and healthy—per capita world product in 2100 is \$3,000 (1970 US dollars) and the world average life expectancy is more than 75 yr; (4) natural resources are in a more favourable long term position. It must be noted that these favourable results depend not only on the rational economic policies proposed here, but also on the important technological advances proposed by Meadows and cited previously.

The economic policies are typical of those already in force in the developed nations. Strong governmental regulation in agriculture has a particularly long history. A positive subsidy on land development and a negative subsidy on over-production on developed land are well within the framework we know. Market mechanisms that regulate investment through demand are an essential part of the industrial system. At worst, the simulated mechanism might require a curtailment on that advertising which has as its aim the encouragement of conspicuous consumption.

Research for Improvement

There is already extensive research under way in each of the technological areas where improvements are needed—exploration for resources, energy supply, recycling, pollution control, agricultural technology, birth control and family planning. In the past, research has achieved improvements comparable in level to the doubling (of resources) and reduction by a factor of four (of pollution) used in the Meadows model, but these have required time. To estimate the effect of a research delay, a run was made in which the technological advances in recycling, pollution, land yield and birth control were not introduced until the turn of the century—a delay of 25 yr. Qualitatively, the simulation results were comparable to those shown in Fig. 2, but the few years with-

out the technology made a definite difference; there were an extra 1,000 million people by 2100 and resources were down by 25% from that of Fig. 2. Clearly the technology is needed, and the sooner the better, but considering the coarse nature of the model, the real conclusion is that a well directed programme of technological development accompanied by rational economic policies offers reasonable hope of a satisfactory transition to a stabilized comfortable world. To be sure, resources will be depleted substantially by the year 2100, but the society of that time will have known more than 75 yr of prosperity based on stability rather than growth. They will have had plenty of time to plan their future.

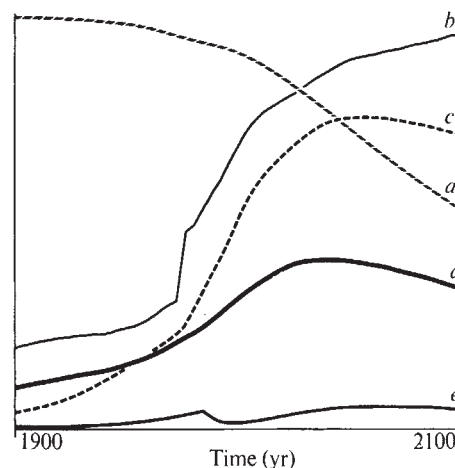


Fig. 2 Results of simulation which incorporates two revised economic policies to avoid the overshoot modes in Fig. 1. A stable prosperous world is reached. Scales and annotation as in Fig. 1.

The Meadows model, when corrected and provided with revised economic policies, indicates hope for technological solutions to a few of the problems in the present world, but this does not resolve the disturbing questions raised by men of many disciplines^{6,7}. The gross level of aggregation in the Meadows model is appropriate for an overview of the questions of population, resources and environment, but it leaves a great many small scale situations with potentially dangerous consequences for man unsimulated. Then, on the global scale, many critical human issues are left out, for example, the unbalanced distribution of wealth and resources in the world; the degradation of the human spirit that has accompanied the industrial revolution; and international conflict among nuclear powers. One hopes for similarly encouraging prospects from simulations which include these factors.

I thank Drs J. Hall, P. Boyce, O. Franz, G. Gilbert, K. Pearson and E. Walther for their help, and the MIT team for providing copies of the original program and working papers. In so doing, they are true to their word, "... every assumption we make ... is open to criticism by all" (ref. 2, page 22).

¹ Forrester, J. W., *World Dynamics* (Wright-Allen Press, Cambridge, 1971).

² Meadows, D. L., et al., *The Limits to Growth* (Universe Books, New York, 1972).

³ Passell, P., Roberts, M., and Ross, L., *N.Y. Times Book Review* (April 2, 1972).

⁴ Klein, R., *Commentary*, 53, 6 (1972).

⁵ Meadows, D. L., *op. cit.*, 140, Fig. 42.

⁶ Commoner, B., *The Closing Circle* (Knopf, New York, 1971).

⁷ Galbraith, J. K., *The New Industrial State* (New American Library, New York, 1967).

Comparison Between Ice Age and Present General Circulations

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Small reductions of tropical sea surface temperatures during ice ages are associated with substantial reductions in latent heat release and in the temperature of the upper tropical troposphere. Numerical simulations confirm that this reduced the mean baroclinicity during ice age winters and presumably the atmospheric heat transport from low to high latitudes. The computed wind driven ocean circulation was also weaker. Local heat balance considerations suggest that ice age cloud cover over the tropical oceans was more extensive in spite of reduced evaporation and precipitation. The same deduction is suggested by analytical arguments about atmospheric convection.

SEVERAL investigators¹⁻³ have used sediment analysis to reconstruct the distribution of sea surface temperatures during glacial ages. A convenient set of maps, reproduced here as Fig. 1, was prepared by project "Climap" scientists and published in the National Science Foundation Annual Report for 1972. Figure 1 shows a difference of more than 10° C between present and ice age surface temperatures north of the 50th parallel in the North Atlantic. By contrast, the change in the Caribbean and in the tropical Atlantic amounts to only 3° or at most 4°. Over continents, the difference is even larger, with summer surface temperatures in the once glaciated regions of Europe and North America today some 30° warmer than they were 17,000 yr ago.

Clearly, the mean meridional temperature gradient at the bottom of the atmosphere was larger during ice ages than now. From this it has been commonly assumed that ice ages were characterized by a more vigorous atmospheric circulation and by an increased meridional heat transport. Contrary to this conventional wisdom, I suggest that the opposite may have been the case.

The atmospheric circulation is driven to a large extent by the release of latent heat, supplied originally to the trades by the tropical and sub-tropical oceans. The trades form the lower, horizontal branch of the Hadley circulations. These can be conceived as two vortex rings which encircle the globe north and south of the equator. Over the Indian and South Atlantic Oceans the Hadley circulations are coupled with the Indian and African monsoon.

The rising branch of the Hadley circulation forms the Inter-tropical Convergence Zone (ITCZ). Within this zone and also in hurricanes, air ascends directly without much dilution from the sea surface to the tropopause in tall cumulus towers. After reaching the vicinity of the tropopause it spreads out and sinks down over an area which is a hundred to a thousand times larger than the cross-sectional area of the rising currents. Air which has been in contact with the tropical oceans fills in this way a large part of the whole

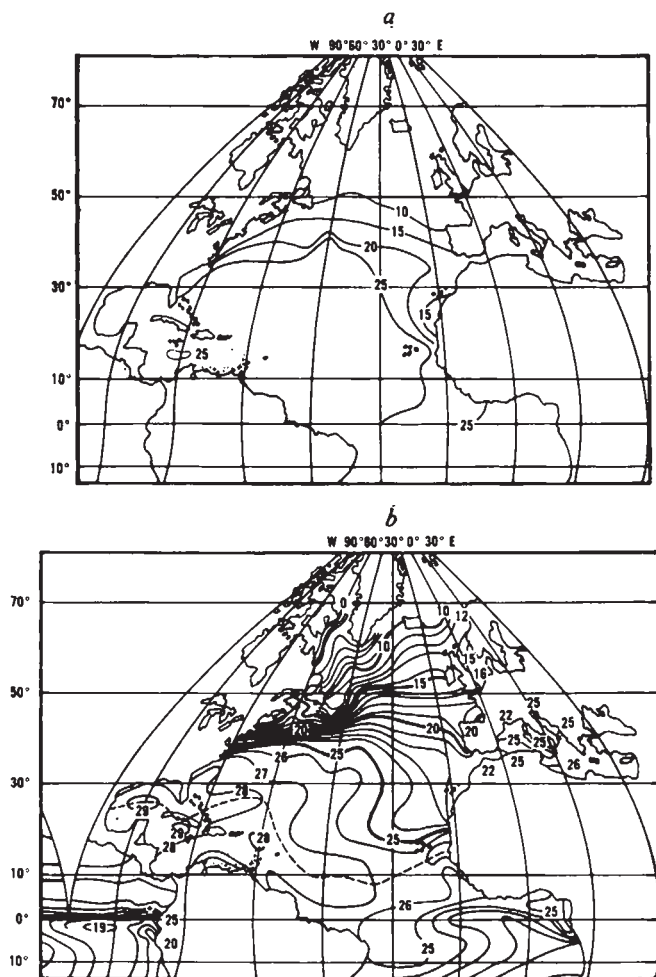


Fig. 1 North Atlantic sea surface temperature maps reconstructed by "Project Climap" scientists for, a, summers 17,000 yr ago and, b, for modern summers.

tropospheric volume—just as the water which sinks in the Antarctic and spreads out along the ocean bottom determines the temperature of a large oceanic volume.

During the undiluted rapid ascent of air in tropical cumulus towers, the so-called equivalent potential temperature θ_e is conserved.

$$\theta_e = \theta^L (c_p T) \quad (1)$$

where θ is the potential temperature (that is the [absolute] temperature which the air would have if brought adiabatically to sea level pressure), r is the humidity mixing ratio, L the latent heat of evaporation, c_p the specific heat at constant pressure and T the temperature. The saturation mixing ratio—the maximum amount of vapour which the air can hold—is an approximately exponential function of the temperature. This has a strong effect on the value of θ_e . Air at a pressure of 1,000 mbar, which is in thermal equilibrium with water at $\theta = 301$ K, has an equivalent potential temperature $\theta_e = 373.8$ K; if the water is three degrees colder ($\theta = 298$ K) then $\theta_e = 357.7$ K.

As the air ascends the water vapour is condensed and precipitated. The heat of condensation is used to increase the potential temperature θ . In the upper troposphere the mixing ratio r of the ascending air has become very small. The exponent in equation (1) then differs from one by less than 0.002, which makes the potential temperature θ there nearly equal to the equivalent potential temperature θ_e . So after the condensation of all the vapour, air which had been in contact with a sea surface at 25° C could have become 16° colder than air which had been in contact with a surface at 28° C.

In reality, the air which is lifted upwards in tropical cumulus towers is not fully saturated initially nor can it ever reach a level where all the vapour is condensed. A relative humidity of 85% is reasonably representative for air near sea level in tropical storms. If such air, at an initial temperature of 25° C, was lifted to the 200 mbar level (approximately 12 km) it would arrive there with a temperature which would be about 10° colder than air at an initial temperature of 28° C.

One can expect a roughly three-fold amplification of tropical sea surface temperature changes in the upper troposphere. Above colder water this amplification becomes much smaller. At an initial sea temperature of 17° C, a change by 1° would be amplified only about twice with height. Below 10° C the amplification becomes practically negligible.

In any case, air is not lifted directly from the sea surface to 200 mbar over the temperate oceans. In the Hadley circulations, the air spirals round axes which, if not horizontal, have at least a marked horizontal tilt. Conditions are quite different in higher latitudes, where the deflecting force of the Earth's rotation is stronger. Heat is carried polewards there chiefly by baroclinic eddies—travelling cyclones and anticyclones. These are quasihorizontal circulations around vertical axes, which do not permit any significant direct transport of air from the sea surface to the tropopause. So local changes in sea-surface temperatures in extratropical regions do not have the controlling effect upon conditions, which exists in the tropics.

Nor can radiation exert such a control. The albedo of ice and its low conductivity can cause very low temperatures on the surface of snow and ice fields, but the effect on the atmosphere is largely restricted to the adjacent air layers, without much influence on higher strata. At the 200 mbar level the air above the polar ice caps seems to be almost insensitive to the temperature of the surface below. In summer it tends to be warmer than equatorial air at the same level, even though the surface temperature cannot rise above freezing.

During an ice age with even slightly colder tropical oceans, the upper equatorial troposphere must have been substantially colder. From the presumed approximate invariance of the temperature at the same level in higher latitudes, it follows that the mean meridional temperature gradient in the

upper troposphere was probably weaker during an ice age than today.

Zonal Circulation

Large temperature differences between low and high latitudes can be maintained only by the centrifugal pumping action of an upward increasing mean westerly wind u . This is expressed by the thermal wind relation

$$\partial u / \partial z = (g/f) \partial T / T \partial y \quad (2)$$

($\partial u / \partial z$ = vertical shear of zonal wind, f = Coriolis parameter, $\partial T / \partial y$ = mean meridional temperature gradient). Large values of the wind shear are equivalent to a large storage of available potential energy by the atmosphere. The resulting "baroclinic instability" gives rise to "synoptic scale" disturbances. These convert the available potential energy which had been pent up by the zonal flow into the kinetic energy of the extratropical eddies which carry heat from low to high latitudes. The resulting heat flux reaches its highest values in the upper troposphere between latitudes of 30° and 40° (ref. 4). The value of the wind shear in that region can serve therefore as a rough measure of the baroclinic instability. The preceding argument suggests that the wind shear in the upper troposphere may have been lower during an ice age than it is now. This is confirmed by numerical experiments.

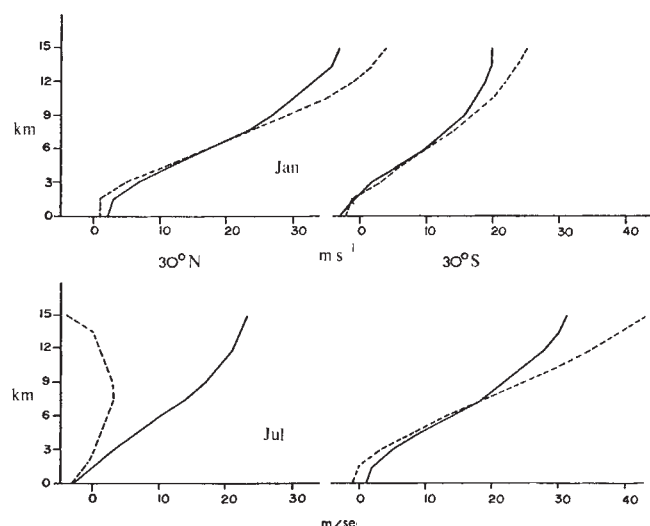


Fig. 2 Vertical profiles of the mean zonal wind component at 30° as derived from the NCAR general circulation model for ice age surface conditions (—) and present conditions (---).

Williams *et al.*⁵ have used the NCAR general circulation model to simulate the global atmospheric motion that might have been associated with surface boundary conditions existing some 20,000 yr ago. The model covers the whole globe with a resolution of 3 km in height and of 5° in latitude and longitude, except for the polar regions. The heat sources and sinks which force the simulated circulation are caused by the differential absorption and emission of radiation and by transfers across the lower boundary. Cloudiness is computed as a function of the model state at the 3 km and 9 km levels.

The model was integrated for four cases, with the sea surface temperatures, snow lines and radiation inputs that are characteristic for the months of July and January during ice ages as well as for present boundary conditions in the same months, to provide a control. Topographic changes associated with the presence of the ice caps and with the resulting sea level reduction were allowed for. The integration was continued for 80 d in each case. The last 30 d of these simulated developments were then used to generate four different

monthly statistics. This procedure was designed to minimize the effect of the initial conditions upon the monthly averages.

Figure 2 shows the simulated vertical distribution of the zonally averaged westerly wind components in the four cases. The slope of the graphs indicates the vertical shear. During winter in both hemispheres the simulated ice age wind shear is indeed weaker than the one which is calculated to exist now. The same difference characterizes the southern summer. During the northern summer, however, the modern calculated wind shear is weaker than the ice age shear. This means that ice age summer conditions were more similar in the two hemispheres than today. In the model this is reflected by active cyclonic activity during the glacial summer.

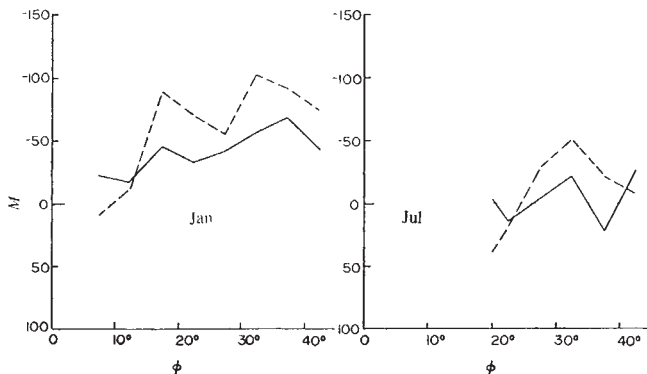


Fig. 3 The Sverdrup mass transport in the North Atlantic Ocean as derived from the NCAR general circulation model for ice age conditions (—) and present conditions (---). The transport M_y is specified in Sverdrups ($1 \text{ Sverdrup} = 10^6 \text{ m}^3 \text{ s}^{-1}$) as a function of the latitude ϕ .

It would be unwise to read too much into the numerical results. Particularly during summer, the realism of the model in low latitudes is questionable. As far as the results go, they do suggest that the difference between present and ice age upper tropospheric temperatures is largest above the once widely glaciated zones of the northern hemisphere during the summer season. Apart from that, however, the difference between upper air temperatures now and then is larger above the tropics than anywhere else. The heat transport by the baroclinic eddies is directed principally into the winter hemisphere. Computations to calculate this flux will be made later. In the meantime, the graphs in Fig. 2 suggest that ice age upper baroclinic instability in the southern hemisphere and during the northern winter was weaker than it is now. The associated heat flux reduction may well have contributed to the maintenance of glacial conditions in high latitudes.

Oceanic Heat Transport

The meridional heat transport by ocean currents was also probably lower during the ice age than it is today. This can be expected *a priori*, because the present warm North Atlantic drift currents would probably not allow Ireland to become glaciated, nor would they allow ice to drift as far south as the presence of ice rafted debris indicates to have been the case⁶. The same inference can be drawn from the shape of the isotherms in Fig. 1. In fact, sediment analysis led McIntyre¹ and Briskin⁸ directly to the stipulation of a much reduced meridional extent of the Gulf Stream system during ice ages. This deduction is supported, at least qualitatively, by the numerical simulation.

Having been designed originally for the study of relatively short term weather developments, the NCAR model simulates only atmospheric motion. It allows for the determination of surface temperature variations over land and ice

as a function of the transient local energy balances and the conductivity of the underlying material, but requires sea-surface temperatures to be specified. It cannot be used, therefore, for the modelling of long term climatic fluctuations. But one can use the simulated surface wind to obtain some information about the matching wind driven ocean circulations.

A large part of the oceanic contribution to the meridional heat flow can be associated with the Sverdrup transport, particularly in the northern hemisphere. This process causes water to move towards the equator if the wind exerts an anticyclonic torque upon the surface.

$$m_y = \beta^{-1} \text{curl } \tau \quad (3)$$

where m_y is the vertically integrated mass flow per unit width of ocean, β represents the meridional variation of the Coriolis parameter and τ is the wind stress vector. In subtropical and temperate latitudes the Sverdrup transport towards the equator increases with the vector difference between the surface westerlies and the trades. It is compensated by western boundary currents such as the Gulf Stream and the Kuroshio which flow in opposite directions along the edge of the continent. Although Sverdrup transports may not account fully for the mass flow in the Gulf Stream, they provide a theoretical lower limit which is of the right magnitude and which can be used to estimate variations in the oceanic meridional heat flow.

The model generates numbers for the wind components u and v a few metres above the sea surface at all grid points. The so-called bulk-aerodynamic relation can therefore be used to obtain the stress components

$$\tau_x = \rho C u \sqrt{(u^2 + v^2)} \quad \tau_y = \rho C v \sqrt{(u^2 + v^2)}$$

where ρ is the surface air density and the non-dimensional drag coefficient $C \approx 1.3 \times 10^{-3}$. The derived values of m_y/ρ were integrated across the width of the North Atlantic along the different parallel circles and the result M_y is shown as a function of the latitude ϕ in Fig. 3.

The modern transport values shown in Fig. 3 are rather large compared with those derived from wind observations. Indeed, they are larger than the actual Gulf Stream transport. During modern July, the model produces south of 15° northern latitude a pronounced drift towards the north, which would have to be balanced by a very strong ($10^8 \text{ m}^3 \text{ s}^{-1}$) southward moving boundary current. This is quite unrealistic. It has not been reproduced here, as this would only confuse the picture. It confirms the apparent difficulty of the NCAR model in attempting to reproduce conditions in the inner tropics during summer.

Allowing for these reservations, the computations do reveal that the wind driven mid-latitude mass transport in the North Atlantic was considerably weaker during the ice age than it is now. This implies a reduced northward flux of warm water in accordance with the sediment studies quoted above.

Sea-surface Temperatures and Clouds

What were the conditions which could maintain a colder tropical ocean surface? The local heat balance of the ocean can always be expressed in the form

$$R_s = R_i + F + \int_B^0 H dz \quad (4)$$

where R_s is the absorbed solar radiation flux per unit of sea surface, R_i is the net upward infrared radiation flux and F is the sensible and latent heat flux to the atmosphere. In the tropics the latter is usually about an order of magnitude larger than the former. The last term in equation 4 represents the vertically integrated divergence of the horizontal oceanic heat flux. The flux through the ocean bottom at B is negligible in the present context.

During an ice age, when the sea was colder, the infrared radiation loss R_i and the latent heat loss F were both pre-

sumably smaller. The argument of the previous section indicates that the export of heat from the tropics by ocean currents was also reduced. To satisfy the heat balance requirements one must conclude that the amount of solar radiation R_s which reached the sea surface, cannot have been as large as today. In other words I expect that there must have been a more widespread cloud cover at that time. This expectation is supported by analytical inferences and numerical simulation.

Clouds increase the albedo and hence reduce the planetary temperature. They diminish both the radiation flux which reaches the sea surface and the net infrared flux which leaves it. The former effect predominates in the tropics and in the temperate zone; in summer it also predominates in high latitudes⁷. Averaged over the seasons, any increase in the amount of low cloud tends to keep the surface cooler, except for the relatively small area above about 60° latitude where clouds act as a blanket which keeps the surface warmer.

The generation of low clouds over the tropical oceans is a function of the temperature structure. As argued above, the temperature of the upper tropical troposphere is largely determined by the equivalent potential temperature at the underlying sea surface. As the air sinks in the descending branch of the Hadley circulation it is cooled by infrared radiation at a rate $R \approx 1.5^\circ \text{C d}^{-1}$. The mean observed vertical gradient of potential temperature $\partial\theta/\partial z$ in the sinking air is about 5°km^{-1} . It follows that the subsidence velocity

$$W \sim R/(\partial\theta/\partial z) \sim 0.3 \text{ cm s}^{-1}$$

At low elevation, the subsiding air is usually colder than the sea surface below. The resulting convective mixing of the lowest air layers produces a more or less constant potential temperature distribution along the vertical in the trades, immediately above the oceans.

I now consider two air masses which have reached equilibrium with two hypothetical ocean surfaces characterized by $\theta=295 \text{ K}$ and $\theta'=299 \text{ K}$. They will then have the equivalent potential temperatures marked θ and θ' in Fig. 4. The air is subsequently lifted to levels where the mixing ratio is reduced to 0.6 g kg^{-1} . These levels are marked by h and h' . If the air sinks and is cooled at the same rate in the two cases, the colder air must reach its initial potential temperature at a higher elevation. The well-mixed tradewind layer which extends from that level to the surface is therefore deeper. This favours cloud formation.

This argument suggests an increased cloud cover over the ice age tropical oceans. How does this tally with the presumed decrease in evaporation from the colder tropical oceans and with the necessarily associated reduction of precipitation? The latter seems to be confirmed by geological observations which indicate an increased low latitude aridity during the height of the most recent ice age^{8,9}.

The answer to the apparent paradox of less precipitation from more clouds may lie in the change that occurs with temperature in the residence time of water vapour in the atmosphere—in other words in the ratio of atmospheric water storage to precipitation. When the sea surface temperature is low, less water is supplied to the air, but with decreasing total moisture content, the convective instability of the atmosphere and the liquid water content of clouds decreases even more. This makes the precipitation generating mechanism less efficient. It can cause the volume averaged relative humidity—the ratio of actual atmospheric moisture to capacity storage—to be smaller during a warm climatic regime than during a cold regime.

Cloud generation in the NCAR model depends on the vertical velocity and on the relative humidity. As the latter tends to become larger over cold ocean surfaces, one finds necessarily that the model also produces more low clouds during an ice age. At the same time it generates less precipitation and evaporation than it does with modern boundary conditions⁵.

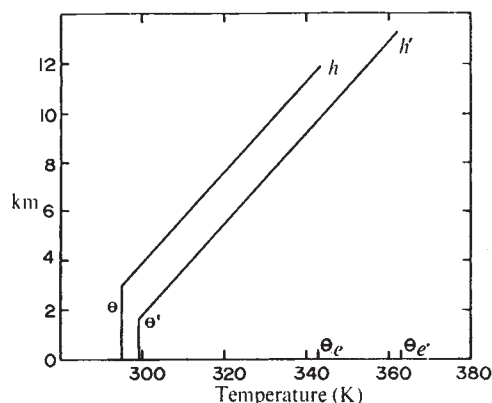


Fig. 4 The vertical temperature distributions (schematic) of the tradewind region expected to be associated with mean sea surface temperatures of $\theta=295 \text{ K}$ and $\theta'=299 \text{ K}$. The heights h and h' represent the levels at which saturated air, rising from sea level, would have a mixing ratio of 0.6 g kg^{-1} .

The relationship between ocean surface temperature, global low cloud amount and precipitation has also been studied with the same model by Schneider and Washington at NCAR. Their study has not yet been published, but they gave permission to quote some pertinent numbers (Table 1).

Table 1. Stipulated Change in Global Ocean Surface Temperature (ΔT_0) and the Resultant Changes in Global Relative Humidity ($\Delta r.h.$), Low Cloud Cover (Δn), Global Mean Temperature at 3 km (ΔT_3) and Precipitation ($\Delta pr.$)

$\Delta T_0 (^\circ \text{C})$	-2°C	$+2^\circ \text{C}$
$\Delta r.h. (\%)$	$+1.17$	-3.33
$\Delta n (\%)$	$+1.53$	-2.74
$\Delta T_3 (\%)$	-3.6	$+3.8$
$\Delta pr. (\text{mm per } 90 \text{ d})$	-36.7	$+39.7$

The data of Table 1 illustrate not only the inverse relationship between global cloud amount and precipitation changes, but also the amplification of sea-surface temperature changes with height which can be expected from the tendency to conserve equivalent potential temperature.

Further Problems

This article essentially compares two stationary climatic regimes. It does not reveal anything about the process and causes of climatic change. The analysis at least raises the question, however, whether slight changes in the surface temperature of the tropical oceans might not induce the more dramatic changes at higher latitudes—rather than the other way round as is usually assumed.

Although the numerical results provide suggestive supporting evidence for the observational and analytical findings, they cannot be accepted without some reservation. The ability of the NCAR model to represent low level winds and clouds in the tropics could be better, particularly in summer. In any case, the simulation of climate as a dynamic process can be achieved only with a combined atmosphere/ocean model which was not available for the present study. It is reasonable to assume, however, that even the present model is able to indicate the sign or the general character of circulation changes that would be caused by a change in the real boundary conditions.

The arguments presented above seem to hang very well together. It is almost inevitable that changes in tropical sea surface temperature must lead to amplified changes of the

same sign in the upper troposphere above. It is almost equally certain that a colder tropical sea surface must have been associated with an increased cloud cover. In the immediately preceding section, I argued that these two phenomena are connected. It seems probable, but less certain, that the colder tropical troposphere was associated also with a reduced baroclinicity. The contention would be more convincing if supported by a more detailed modelling of the infrared radiation flux which is associated with different surface temperatures. These studies are planned for the near future. The suggestion that the wind-borne and current-borne meridional heat flux was weaker during an ice age than now may appear to be even more debatable. It is supported, however, by the stipulated reduced baroclinicity, by the numerical simulation and by the oceanic observations.

I thank Jill Williams, Dr Steve Schneider and Dr Warren Washington at the National Center for Atmospheric Research for lending me tapes used for the computation of the Sverdrup transports, and for supplying the numbers in Table 1. Jill Williams and Dr Schneider helped me with

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Relative and Latitudinal Motion of Atlantic Hot Spots

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Although not all hot spots are fixed with respect to one another, the members of small groups of them seem to be fixed internally.

THE hypothesis that hot spots¹ and their underlying plumes² all remain fixed with respect to one another, and perhaps also to the Earth's spin axis and axial dipolar magnetic field, has recently received attention³⁻⁵. Atwater and Molnar⁶ have shown, by rotating plates back to their 13 and 38 m.y. position, that some hot spots (notably Iceland and St Paul/Amsterdam) have probably moved with respect to one another during this time. Using a different approach we present here evidence that during the past 120 m.y. some hot spots have moved significantly with respect to each other and to the magnetic field.

We use the term "hot spot" to describe succinctly a class of localized volcanism and associated uplift characteristically found within plates (Hawaii and Tibesti, for example), but also found on divergent plate boundaries (Iceland, for example). The term is used to describe the surface feature, with no intended implications about processes below the surface, in the same way as the term "island arc" is used. In the ocean a hot spot trace is a volcanic ridge or line of seamounts which leads away from a hot spot and which is considered to have been progressively generated as the plate moved relatively over or away from the underlying source of the hot spot. Where a hot spot occurs on a spreading ridge axis, a trace is generated on each plate. The former presence of a hot spot on continental crust is expressed by relatively localized alkaline volcanic piles or subvolcanic alkaline intrusives,

sometimes accompanied by more extensive flood basalts. The former position of a hot spot at any time in the past is marked by the point of that age on its trace.

Misfit

Figure 1 is a reconstruction of the Atlantic ocean and its surrounding continents about 120 m.y. ago⁷, and five selected Atlantic hot spots which possess comparatively well defined traces are plotted on it at the positions that they occupied at that time. If hot spots stay fixed with respect to each other, it should be possible to superimpose the same hot spots in their present relative positions on their positions 120 m.y. ago. It is not possible to do this, and the misfit is conveniently represented by keeping one hot spot fixed, and plotting the others in their present positions relative to it. We have chosen to keep the Colorado Seamount hot spot fixed for the purposes of illustration, as it has a trace on the North American plate, and the reference frame on Fig. 1 is with respect to present North America. Although the Azores hot spot does plot at the relative position it occupied 120 m.y. ago, the three others shown from the South Atlantic fall about 20° beyond their positions at that time. This indicates that relative motion between them and the two northern hot spots has occurred at an average rate of 1.8 cm yr⁻¹ during the past 120 m.y., in a direction approximately perpendicular to the general direction of relative plate motion.

Data used to plot the hot spot positions on Fig. 1, and for subsequent parts of this paper, are listed in Table 1. The positions of the two northern hot spots at 120 m.y. ago were picked from maps of seafloor age in the central Atlantic^{7,8}. A certain amount of interpolation has been necessary for the Colorado Seamount hot spot traces. The early part is well defined only on the western side, and

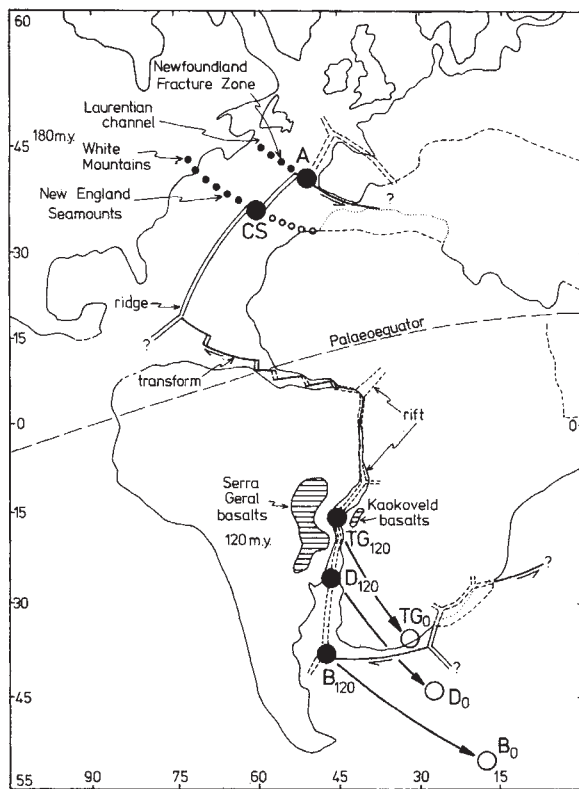


Fig. 1 Sketch of configuration of Atlantic continents, with schematic plate boundaries, for about 120 m.y. ago (from ref. 7); reference frame fixed to North America. ●, Positions of five hot spots at this time as given by their traces; ●, earlier parts of traces of the two northern hot spots; ○, an interpolated older trace (see text); ○, present positions of the southern hot spots relative to Colorado Seamount hot spot kept fixed at its position relative to North America 120 m.y. ago. A, Azores; CS, Colorado Seamount; TG, Tristan da Cunha/Gough; D, Discovery Seamounts; B4, Bouvet. Large arrows indicate total motion of the three southern hot spots between 120 m.y. ago and the present relative to Colorado Seamount hot spot. Palaeoequator is around average pole at 69° N 180° W with respect to North America.

the later part only on the eastern side of the Mid-Atlantic ridge, but the age ranges of the partial traces overlap, so the interpolation is valid. Some authors (for example ref. 9) prefer to generate the New England (Kelvin) and Corner Rise seamounts from the Azores hot spot. We do not favour this, because partial closure of the central Atlantic by appropriate rotations⁸ connects the Corner Rise seamounts with a point of the same age on the trace of seamounts running east from Colorado Seamount.

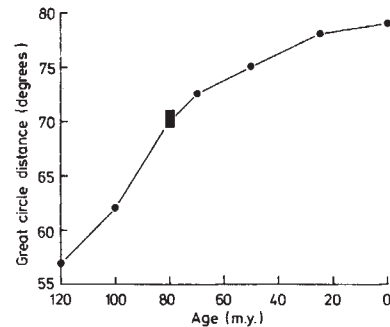


Fig. 2 Great circle motion between Colorado Seamount and Tristan/Gough hot spots during the past 120 m.y.

The relative motion between the five hot spots is set out in Table 2, showing in quantitative form what we show diagrammatically in Fig. 1. The large motion between the two groups of hot spots is clear, but there does not appear to have been significant motion between the hot spots in each group.

Relative Motion

The average rate of relative motion between the two groups has been about 1.8 cm yr⁻¹, but this rate has not been constant. Points representing particular ages on the traces from Colorado Seamount and Tristan/Gough can be picked from maps of seafloor age in the central^{7,8} and

Table 1 Position and Palaeolatitude Data for Some Atlantic Hot Spots

Hot spot	Trace	Position of hot spot 120 m.y. ago	Present coordinates of hot spot	Present coordinates of hot spot position 120 m.y. ago	Palaeolatitude of position of hot spot 120 m.y. ago	180 m.y. ago
Azores	Newfoundland Ridge (or "Fracture Zone"); (eastern trace in tectonized area)	South-east corner of Grand Banks	38° N 27° W	41.5° N 48° W	26° N	29–30° N
Colorado Seamount	New England Seamounts; Corner Rise Seamounts; ill defined to present Mid-Atlantic Ridge	South-eastern New England Seamounts on Bermuda discontinuity	34° N 37.5° W	36.5° N 59° W	25° N	25–27° N
Colorado Seamount	Interpolated from continental margin to Great Meteor Seamount; Cruiser Seamount—Mid-Atlantic Ridge	Just west of Azores—interpolated	34° N 37.5° W	29° N 19° W	25.5° N	
Tristan da Cunha	Rio Grande Rise	Florianopolis	37° S 12.5° W	27° S 48° W	29° S	
Gough Island	Walvis Ridge	Cape Fria	40° S 10° W	18.5° S 11.5° E	30° S	
Discovery Seamounts	Poorly defined line of seamounts	Luderitz	47° S 6.5° W	27° S 14° E	39° S	
Discovery Seamounts	None known except one seamount just off continental margin	East of Montevideo	47° S 6.5° W	35.5° S 53° W	38° S	
Bouvet Island	Meteor Seamount chain	South of Cape Agulhas	54.5° S 3.5° E	35° S 18° E	48° S	
Bouvet Island	North Falkland Plateau; ill defined to east	South-west Argentine Basin—interpolated	54.5° S 3.5° E	45° S 59° W	48.5° S	

southern^{10,11} Atlantic. This identification of the age points along the two traces assumes that the two hot spots have stayed approximately on the axis of the spreading ridge, and is justified because hot spot traces extend away on both sides of the spreading ridge. Data are given in Table 3 and the change in great circle distance with time is shown in Fig. 2. Although the shape of the curve showing the relative motion is crudely exponential, we do not attach significance to this, since it only concerns the motion between two of many hot spot groups. We think, however, that the variations in the rate of motion are significant, and this rate has varied between about 5 cm yr⁻¹ (100 to 80 m.y.) and about 0.5 cm yr⁻¹ (25 to 0 m.y.). It is intriguing that the time of maximum rate of relative motion coincides with a time of world wide accelerated spreading rates⁷, but we have not been able to confirm this correlation for any other hot spots.

We take the Mascarene/Chagos-Laccadive Ridge and most of the Ninety-East Ridge to have been produced during the past 65 m.y. by the two hot spots now at Mauritius/Réunion and St Paul/Amsterdam Islands respec-

tively. Tentative age data at two places along each of these traces^{12,13} suggest that at present these two hot spots have the same separation as they had 65 m.y. ago (about 25°), but that their separation was slightly greater (about 29°) 25 m.y. ago. No significant motion between the Mauritius/Réunion and the Tristan/Gough hot spots can be detected for the past 12 m.y. (ref. 14); the motion between 12 m.y. and 65 m.y. ago must amount to about 6° towards each other, on the basis of established plate motions¹⁵.

Ideally, palaeomagnetic data can be used to establish how the relative motion between the hot spots has been distributed with respect to the magnetic field and by inference to the spin axis. We have estimated average palaeomagnetic poles for various plates at particular times from data contained in a recent compilation¹⁶. We used only non-redundant poles in reliability category A, and only if the age of any pole is well defined to within 10 m.y. of the age required (exceptionally 20 m.y. for the 180 m.y. and 120 m.y. ages), and we excluded poles from areas that may have suffered subsequent tectonic displacement. As

Table 2 Great Circle Distances between Hot Spots

Hot spots	180 m.y.	120 m.y.	Present	Difference between 120 m.y. and present
Azores-Colorado Seamount	10	10	9	-1
Colorado Seamount-Tristan da Cunha	—	57	75.5 77	+20 ± 2
Colorado Seamount-Gough Island	—	9	79 (7 to)	-2 to +1.5
Gough Island-Discovery Seamounts	—	19	16.5 18.5	-2.5
Gough Island-Bouvet	—	9.5	10	-0.5
Tristan da Cunha-Bouvet	—		20.5	+1.5
Discovery Seamounts-Bouvet	—		10	+0.5

All measurements in degrees (1 degree ≈ 110 km).

Table 3 Increments of Motion between Tristan/Gough and Colorado Seamount Hot Spots

Age (m.y.)	Present coordinates of hot spot position at ages given				Great circle distance (degrees)	Rate of motion cm yr ⁻¹
	Walvis Ridge-Gough		Colorado Seamount eastwards			
120	18.5° S	11.5° E	29° N	19° W	57	2.8
100	25° S	6° E	29-29.5° N	23-24° W	62	4.1 to 5.0
80	32° S	2° E	30-31.5° N	29° W	69.5-71	1.6 to 3.3
70	34° S	3° W	32.5° N	30° W	72.5	1.4
50	36° S	5.5° W	33° N	32° W	75	1.3
25	40° S	10° W	34° N	35° W	78	0.44
0	40° S	10° W	34° N	37.5° W	79	

Table 4 Average Palaeomagnetic Poles

Plate	180	120	Age (m.y.) 65-60	50	25
Africa	67.5° N 104° W	55° S 74° E	—	—	90° N
North America	72.5° N 94° E	69° N 180° W	(77° N 114° E ?) 85° N 163° W (ref. 5)	—	—
South America	—	83.5° S 113° W	—	—	—
India	—	—	32° S 100° E	—	—
Indo-Australia	—	—	—	70° S 54° E	76° S 89° E
Eurasia	—	—	77° N 150° E ?	—	?

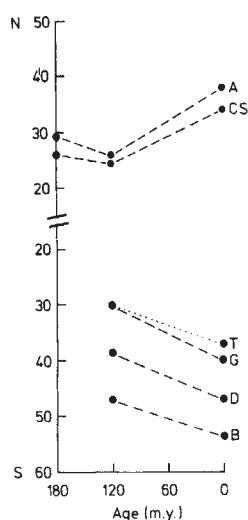


Fig. 3 Latitudinal motion between five Atlantic hot spots during the past 180 m.y. Letters identifying hot spots are as in Fig. 1.

the poles selected have restricted age ranges, any possible polar wandering as distinct from plate motion can be neglected for each age (but not between). Known plate rotations^{8,15,17,18} can then be applied to the groups of poles of each age, and a combined pole defined, which can then be similarly rotated to give a consistent result for each plate.

Palaeolatitudes derived from the average pole for 180 m.y., and perhaps the other average poles, may have errors larger than the differences we are attempting to detect as the selected data scatter over significant areas, up to 15 to 20° across. But as the average poles for 180 and 120 m.y. have been selected and then deliberately rotated so as to be compatible with total subsequent plate motion for those plates involved, palaeolatitudes derived from them may be more reliable than those obtained from separate average poles for each plate, which do not coincide when subsequent plate motion is removed. The average palaeomagnetic poles given in Table 4 should be regarded as present estimates, and only for the restricted age ranges given. No motion of the African plate with respect to the dipole field is required by the palaeomagnetic data for the past 25 m.y. (ref. 19).

Seventeen poles for the Eurasian plate 60 m.y. ago are almost all closely grouped, but the average pole they define is not compatible with an average pole for North America³ when the appropriate North Atlantic motion⁸ is removed (Table 4, in brackets). Three poles in the Eurasian group plot 20° away from the main group, and their position is more compatible with the North American pole. In view of this uncertainty, we have not used the 60 m.y. poles to define palaeolatitudes for the Atlantic hot spots, as the error is potentially as much as 20°. Phillips and Forsyth²⁰ have previously discussed this discrepancy.

Palaeolatitudes derived from average poles are probably of variable reliability and only relatively small changes in one or more of the average pole positions may make a great deal of difference to the inferred motion of particular hot spots with respect to the magnetic field and the spin axis. The palaeolatitudes we derive show that all the hot spots have moved differing amounts with respect to the magnetic field for at least some parts of the last 120 m.y., but the precise amounts for each hot spot we regard as less certain.

Palaeolatitudes of the Atlantic hot spot positions 120 m.y. ago, and for the two northern hot spots at 180 m.y. ago, are given in Table 1. The discrepancies between the palaeolatitudes at 120 m.y. and the present latitudes of the hot

spots are set out in Table 5, and shown graphically in Fig. 3. First, the results show that the total motion between the two groups of hot spots with respect to latitude is nearly as great as their motion with respect to each other during the past 120 m.y., indicating that aggregate relative longitudinal motion has been subordinate, at least for these particular hot spots (see also Fig. 1). Second, each group of hot spots has moved an approximately equal distance away from the equator toward the poles of their respective hemispheres. Duncan and others³ showed that Eurasian palaeomagnetic data for 60 m.y. ago can be interpreted as indicating a large northward motion of the Iceland hot spot (about 20°) since this time. In view of the uncertainty in the palaeomagnetic data, we would suggest that although relative northward motion of this hot spot is probable, the amount of motion may be more modest. We estimate from known plate motions⁸, allowing for uncertainty across the Labrador Sea, that the Iceland hot spot has not moved more than 5° away from the Azores and Colorado Seamount hot spots during the past 60 m.y. On the basis of the North American average palaeomagnetic pole⁵, this indicates no more than about 8° of northward motion of the Iceland hot spot during this time.

Table 5 Latitudinal Motion of Hot Spots

Hot spot (trace east or west)	Latitude/palaeo- latitude change from 120 m.y. to present	Differences between hot spots (degrees)
Azores (W)	12° N	+3 to +3.5
Colorado Seamount (W)	9° N	
Colorado Seamount (E)	8.5° N	+16.5 to +19
Gough (E)	10° S	
Discovery Seamount (E)	8° S	0 to -2
Bouvet (E)	6.5° S	
Tristan da Cunha (W)	8° S	—
Discovery Seamount (W)	9° S	
Bouvet (W)	6° S	—

More Hot Spots

We have attempted to extend this study to the two hot spots of Mauritius/Réunion and St Paul/Amsterdam Islands. The palaeomagnetic data perhaps suggest that Mauritius/Réunion has moved northwards about 10° in the past 65 m.y. and that all or almost all of this relative motion occurred before 25 m.y. ago. On the same basis St Paul/Amsterdam has moved northwards about 16° since 65 m.y. ago. If a very tentative estimate is made of its position 50 m.y. ago, extrapolating from a point suggested to be 45 m.y. old¹³ and using the Australian palaeomagnetic pole, it is possible that the overall relative northward motion of this hot spot may have reversed for a while between 50 and 25 m.y. ago.

The only other hot spot for which data are available is Hawaii; the palaeomagnetic data cannot resolve any motion of this hot spot in the past 70 m.y. (ref. 4), but the equatorial sedimentation data⁴ perhaps suggest it has moved slightly southwards²¹, perhaps up to 5° in the past 40 m.y. By implication, the other hot spots on the Pacific plate which seem to be approximately fixed with respect to Hawaii^{2,4} may be moving in a similar manner.

McElhinny⁵ showed that the apparent motion of the Iceland hot spot with respect to the magnetic field³ is more likely to be due to relative motion between hot spots than to a rotation of the mantle containing fixed plumes with respect to the lithosphere as a whole^{3,22}. Our conclusion that some groups of hot spots have moved significantly

with respect to each other confirms this suggestion. The rate of motion between two small groups of hot spots is comparable with rates of plate motion, and has varied by an order of magnitude over the past 120 m.y.; the maximum rate of separation for these two groups appears to coincide with a temporary global increase in spreading rates⁷. The two or three hot spots within each of these two groups do not, however, seem to have moved significantly with respect to their partners for the maximum lengths of time that they can be observed (180 and 120 m.y.). While moving apart and remaining essentially fixed internally, the two groups of Atlantic hot spots seem to have rotated somewhat relative to one another (Fig. 1). Differential motion of hot spots with respect to the magnetic field and spin axis occurs and for the few hot spots we have studied it seems to have been predominantly in a poleward direction, though not all seem to move toward the pole of the hemisphere in which they occur. The poleward motion may also be intermittent, and even reversible. Data from other hot spots are desirable, but it is unfortunate that although there are many hot spots²³, there are few, if any, others that have clearly marked traces with well defined ages along them and that can be observed for comparable periods of time to those in the central and southern Atlantic.

Satisfactory Hypothesis

We think that the idea that deep mantle plumes^{2,24} underlie hot spots is at present the only satisfactory hypothesis available to account for hot spots, especially to explain their persistence as discrete localized anomalies, in some cases for 180 m.y. This is particularly the case for those hot spots which are on the axes of spreading ridges, and which have remained so for long periods; these are epitomized by the hot spots on the axis of the central and southern Mid-Atlantic Ridge. Although these hot spots have moved with respect to one another, and to the position of the spreading ridge at 120 m.y. ago (Fig. 1), they are still on, or near¹⁴, the axis. The jumping of a restricted length of spreading ridge axis is probably a related phenomenon, and in several cases this is clearly associated with hot spots. It may occur repeatedly in a consistent direction, and this leads to apparent asymmetrical spreading²⁵. Examples of ridge axis jumping occur at the Galapagos^{26,27}, St Paul/Amsterdam Islands¹⁵, south of Australia²⁸, and in Iceland²⁹. The inference we make is that whatever is under the hot spots controls the position of the ridge, and not the reverse; the presence of underlying deep mantle plumes seems to us the only available hypothesis that will account for this.

We suggest that within small groups of hot spots, the hypothesis that they are fixed with respect to one another may be valid, especially for short periods of a few tens of millions of years, but which hot spots belong to a particular internally fixed group may be hard to prove. The hypothesis that all hot spots are fixed with respect to one another and form an independent global reference frame is, however, clearly not valid.

The groups of hot spots that we have shown to remain essentially fixed internally have an approximate maximum horizontal dimension of 2,000 km. This is of the same order as the large swells that occur in East Africa and the Red Sea area, which are about 1,500 km across. We interpret the pattern of alkaline volcanism on abrupt topographic and structural uplifts each about 200 km across within these swells as showing the presence of four or five hot spots in each swell. The Cameroon zone also defines an ellipse about 1,500 km across and contains at least six discrete hot spots on uplifts, although a large overall topographic swell is not present. Apart from these examples, it is difficult to make a similar grouping of many of the remainder of the 120 hot spots we recognize, although

some tentative suggestions can be made. Menard²⁹ has recently demonstrated the occurrence of low amplitude positive topographic anomalies 1,000 to 2,000 km across, and without obvious associated hot spots, in the North-east Pacific. We point out that similar large swells without associated hot spot volcanism are especially prominent in southern Africa, although the amplitude of these features is larger, and all but one are in continental lithosphere.

It may be that the large scale swells and internally fixed groups of hot spots reflect conditions at a depth comparable to their horizontal dimensions, and that the smaller uplifts and hot spots, of which there might be only one in some large swells (Hawaii?), reflect conditions at shallower depths. We speculate that the large swell may represent a broad, very slowly upwelling column, and that the smaller uplifts and hot spots within them represent smaller, more strongly heated and more rapidly rising columns within the large slowly rising column. The implications of the poleward motion of the few hot spots we have examined are not clear to us, and we think speculation on this is perhaps unjustified until well distributed data from other hot spots become available. If it is accepted that deep mantle plumes^{2,24} underlie hot spots, then information relating to processes at the core-mantle boundary, and perhaps in the core, might eventually be extracted from the distribution and relative motion of hot spots. Our observations of the motion of some hot spots during the past 120 m.y. indicate that, if hot spots relate to mantle convection, this convection is probably highly complex and perhaps unlikely to be successfully modelled in terms of a small number of Rayleigh-Benard cells.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Early Archaean Age for the Isua Iron Formation, West Greenland

SOME 150 km north-east of Godthaab, on the edge of the inland ice cap, a refolded syncline of mainly basic rocks containing banded ironstones and other rocks of supracrustal origin is enclosed by granitic gneisses (Fig. 1). These gneisses have yielded an Rb-Sr whole-rock isochron age of $3,700 \pm 140$ m.y., indistinguishable from that of the Amitsoq gneisses of the Godthaab area¹. The present metamorphic grade of both the gneisses and the iron formation is upper greenschist to amphibolite facies. There is no published map of the area, but the following geological details are taken from reports by Keto². The total succession of supracrustal rocks is 2 to 3 km thick. The lower part of the succession consists of quartzites and meta-greywackes. These are overlain by garnet-chlorite schists and banded iron formation, including both Fe-oxides and carbonates. The top of the succession consists of greenschist facies metabasites. Bridgwater *et al.*³ suggest that the Isua supracrustals may represent a shallow-water shelf facies.

The age relations of the gneiss and the iron formation are not yet clear from field evidence, because intense deformation has resulted in structurally conformable contacts.

Here we report a Pb-Pb isochron age for several typical banded ironstone samples consisting of alternating, but deformed, bands of magnetite and quartz + grunerite + Fe chlorite, and for one carbonate rock (Table 1). Rocks of this type occur in many Precambrian terrains and are regarded as chemically precipitated sediments⁴. As far as we are aware this is the first time that Pb isotope measurements have been published for rocks of this type.

Techniques of sample decomposition and separation of Pb by electrodeposition followed those developed in this laboratory by J. Arden and N. H. Gale (to be published). Isotopic analyses were performed on a 12-inch solid source mass spectrometer using a silica gel-phosphoric acid activator on

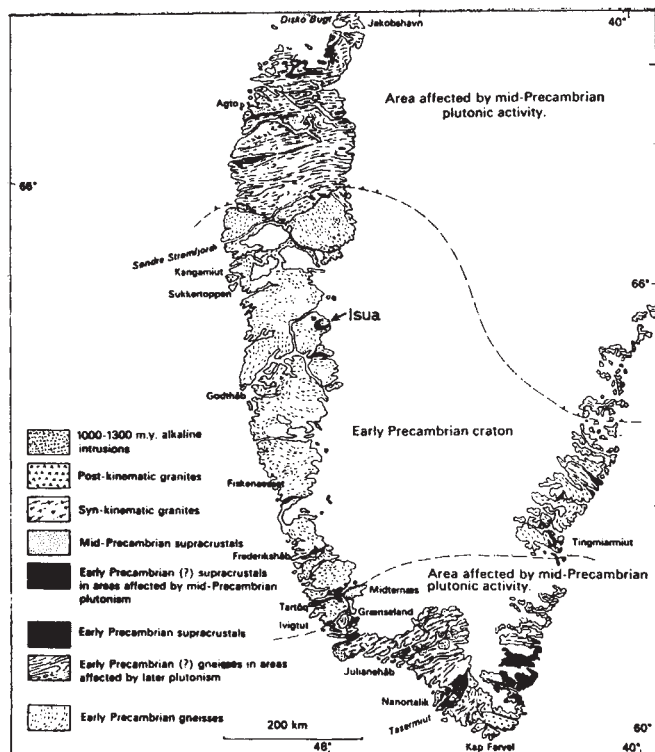


Fig. 1 Geological sketch map of south and southern West Greenland, after Escher in Bridgwater *et al.*³. The locality of Isua is indicated.

single Re filaments. Lead concentrations were determined by isotope dilution with a ^{207}Pb spike, and Pb isotope ratios were measured on separate 0.5 g aliquots. All data were corrected for a 10 ng Pb blank (of assumed modern isotope composition) by iterative calculation, and also for mass fractionation (0.1% per mass unit).

Table 1 Analytical Data

GGU sample No.	Description	$^{206}\text{Pb}/^{204}\text{Pb}^*$	$^{207}\text{Pb}/^{204}\text{Pb}^*$	$^{208}\text{Pb}/^{204}\text{Pb}^*$	Pb (p.p.m.) ^{*†}
15578 (WR)	Fine-grained, banded rock. Bands of magnetite, and grunerite plus quartz	13.834 ± 0.009	14.330 ± 0.01	33.618 ± 0.025	1.228
155781 (M)	Magnetite separated from above sample	12.930 ± 0.013	14.025 ± 0.016	32.671 ± 0.039	0.9012
155781 (S-a)	Silicate fraction from above sample	12.939 ± 0.014	14.042 ± 0.025	33.004 ± 0.053	0.701
155781 (S-b)		12.764 ± 0.006	13.965 ± 0.010	32.724 ± 0.020	0.701
155782 (WR)	Fine-grained banded rock. Bands of magnetite, and grunerite plus Fe-chlorite plus quartz plus calcite	12.932 ± 0.018	14.043 ± 0.019	32.827 ± 0.056	1.808
155783 (WR)	Same as for 155782 (WR)	12.084 ± 0.013	13.738 ± 0.019	32.192 ± 0.071	10.43
		12.073 ± 0.004	13.721 ± 0.004	32.102 ± 0.013	10.47
155784 (WR)	Same as for 155782 (WR)	12.366 ± 0.012	13.785 ± 0.026	32.290 ± 0.052	1.465
		12.360 ± 0.012	13.774 ± 0.015	32.224 ± 0.042	1.466
155789 (WR)	Fine-grained carbonate rock, with disseminated magnetite and accessory grunerite and chlorite	12.155 ± 0.006	13.743 ± 0.008	32.052 ± 0.022	7.633
		12.165 ± 0.011	13.752 ± 0.015	32.095 ± 0.035	7.633

* Corrected for fractionation and blank. Quoted errors are 2σ .

† Pb concentrations were not determined in duplicate, but concentrations have been calculated for duplicate isotope composition analyses where available.

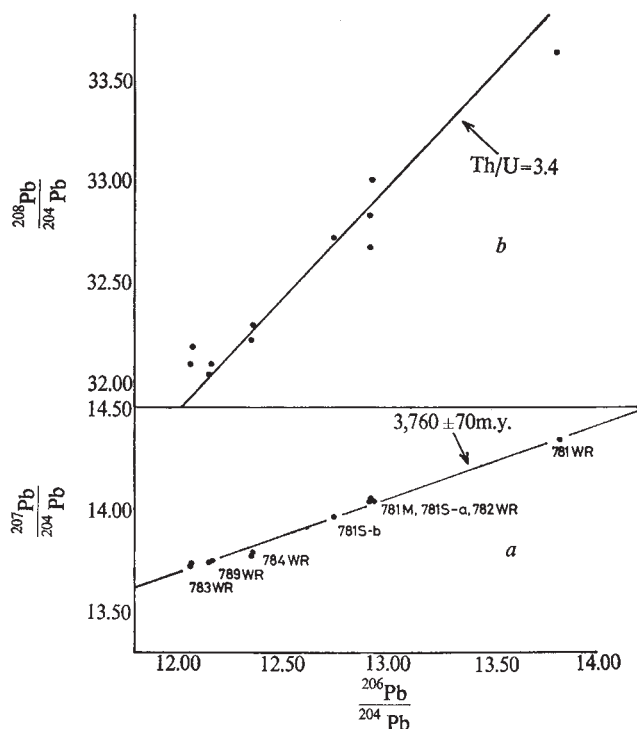


Fig. 2 Pb-Pb plots of analytical data. WR, whole rock; S, silicate fraction; M, magnetite fraction.

The results are presented in Table 1. One pair of duplicate analyses (155781-5) is not in good agreement, possibly due to sample inhomogeneity.

All four banded ironstones (155781, 155782, 155783, 155784), as well as the carbonate rock (155789), were analysed as whole rocks, and a magnetite and a silicate fraction from a separate specimen of 155781 were also analysed.

Figure 2a is a plot of $^{206}\text{Pb}/^{204}\text{Pb}$ against $^{207}\text{Pb}/^{204}\text{Pb}$. The data define a very good isochron (M.S.W.D.=2). A perfect fit is obtained by a 50% increase in errors, and the isochron then corresponds to an age of $3,760 \pm 70$ m.y. (2σ). (λ for $^{235}\text{U} = 9.72 \times 10^{-10} \text{ yr}^{-1}$, for $^{238}\text{U} = 1.537 \times 10^{-10} \text{ yr}^{-1}$, $^{238}\text{U}/^{235}\text{U} = 137.8$). The time-integrated $^{238}\text{U}/^{204}\text{Pb}$ (μ) for the source region of the Pb, assuming a two-stage model of Pb evolution and using the primordial Pb parameters of Oversby⁵, is 9.9 ± 0.1 . Figure 2b is a plot of $^{206}\text{Pb}/^{204}\text{Pb}$ against $^{208}\text{Pb}/^{204}\text{Pb}$. The data scatter about a line giving an average value of Th/U for these rocks of 3.4.

The highly unradiogenic measured Pb isotope compositions demonstrate that these rocks have undergone severe U depletion at or before 3,760 m.y. ago. Uranium depletion is characteristic of many rock types in the West Greenland Archaean, leading to very unradiogenic Pb isotope compositions. This has previously been interpreted as a metamorphic phenomenon⁶. The present samples have not yet been analysed for U. The combined Pb isotope compositions and Pb concentrations (Table 1) indicate, however, that the present day μ value of the rocks would be less than about 0.5, and the U concentrations less than about 0.05 p.p.m. D. Bridgwater (personal communication) reports a uranium content of 0.025 p.p.m. from a sample Isua iron formation (GGU131533) determined by delayed neutron activation.

The value of $3,760 \pm 70$ m.y. is by far the oldest date ever reported for an undoubted water-deposited sediment, or, indeed, for any sediment. It agrees within analytical error with the Rb-Sr whole-rock isochron date of $3,700 \pm 140$ m.y. for the Isua gneisses (λ for $^{87}\text{Rb} = 1.39 \times 10^{-11} \text{ yr}^{-1}$). An unpublished Pb-Pb whole rock isochron date for the Isua gneisses is in close agreement at around 3,700 m.y., although the two-stage, time-integrated μ of the source region of 8.6 is signi-

ficantly lower than the value of 9.9 for the iron formation. (In other words, the present day ranges of $^{207}\text{Pb}/^{204}\text{Pb}$ values are quite different.)

We consider that the 3,760 m.y. date probably represents the date of metamorphism of the iron formation, although a depositional age cannot be ruled out. On the other hand, similar dates from the Isua and Amitsoq gneisses have been interpreted as the time of igneous emplacement or subsequent metamorphism and deformation^{1,5,7}. It could well be that the ironstone formation predates the emplacement of the presumed parent igneous rocks of the Isua gneisses and that it was thermally metamorphosed by them, and/or by the subsequent regional metamorphism. In this connexion, there is no lithological or field evidence to support any suggestion that the ironstone formation is derived by erosion of the gneisses. The significantly different two-stage time-integrated μ values of 9.9 and 8.6 in any case indicate different immediate precursors for these two very different rock formations.

The Amitsoq gneisses of the Godthaabsfjord area contain numerous rafts and enclaves of earlier rocks which represent the oldest material so far recognized in the Earth's crust^{7,8}. The lithology of some of these enclaves strongly suggests that they were originally supracrustal rocks similar to those that occur at Isua, including metasedimentary ironstones.

The high degree of exposure and freshness of the rocks, as well as the great variety of rock types exposed, combine to make Isua one of the most interesting and critical areas in the world for future study of the geological relationships between contrasted rock formations of Early Precambrian age.

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Earthquake Prediction based on Station Residuals

TELESEISMIC residuals of the Matsushiro seismic station clearly indicate a decrease in P-wave velocity underneath this station beginning three years before the Matsushiro earthquake swarm of 1965. This is the first instance where premonitory velocity changes have been observed before

strike slip faulting^{1,2}. It is concluded that P-wave residuals provide another means for assessment of the earthquake risk near seismic stations.

The origin time and location of an earthquake are found by minimizing over all stations the difference between observed and computed arrival time using a standard earth model. As well as random experimental errors the residual at each station is in part due to the imperfection of the earthquake source determination and in part to velocity deviations from the assumed simplified earth model along the ray path. The latter effects are particularly noticeable for rays which travel partly in descending slabs of lithosphere^{3,4} or through volcanic magma chambers. These rays may speed up^{3,4} or slow down⁵.

For the purpose of detecting time variations of the residual due to velocity changes near a station it is necessary to average out effects due to the rest of the paths and the sources. By averaging the residuals at one station from numerous sources in all possible locations the random errors associated with particular paths and particular sources tend to cancel. The part of the residuals due to possible velocity changes in the crust underneath the station will be common to all residuals and can be observed. Nur and Simmons⁶ and Whitcomb *et al.*⁷ have shown that the P-wave velocity changes are more important than that of the S wave. We therefore consider P residuals only.

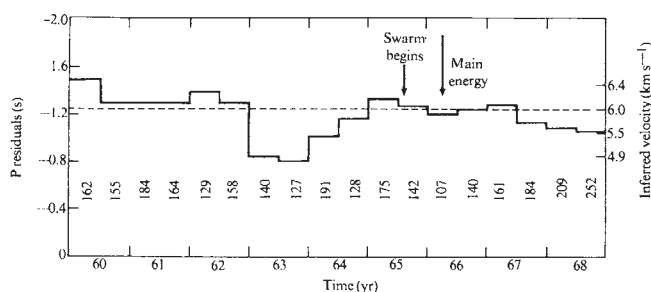


Fig. 1 Teleseismic P residuals during 8 yr at Matsushiro. The numbers of residuals averaged during each period of six months are given in the lower part. ---, Average of the entire period excluding the years 1963 and 1964.

Matsushiro was selected for this study because a large earthquake swarm occurred near and underneath the station⁸ and because this is a good seismological observatory with accurate timing and high gain recording. The total seismic energy released in the Matsushiro sequence was equivalent to a magnitude 6.3 event, and the strain release occurred within a hemisphere of radius approximately 16 km centred at Matsushiro⁹.

A total of 3,000 Matsushiro P-wave residuals (all earthquakes located with approximately twenty-five or more stations) were selected from the *Bulletin of the International Seismological Center* for the years 1960 to 1968. The values of observed minus theoretical travel times were averaged over intervals of six months. These average residuals and the number of events used for each average are shown in Fig. 1.

The deviation of individual residuals from the mean is typically 1 s. Thus, the standard deviations for intervals of six months are expected to be equal to or smaller than 0.1 s because approximately 150 well located earthquakes are available during periods of six months. Calculation of the standard deviation for several intervals showed this to be the case. We therefore expect to detect residual changes if the amplitude and time duration exceed 0.2 s and six months respectively.

The long term average residual of Matsushiro is -1.25 (dashed line in Fig. 1). The values of practically all the

intervals except during 1963 and 1964 are within one standard deviation from the average. In October 1962, the magnitude of the residuals begins to increase, indicating longer travel times. Because all random effects have been cancelled the only cause for the increase can be a decrease in P velocity near the station. The Matsushiro earthquake swarm began 330 d after the residual values were back to normal. The principal energy release of the swarm occurred 570 d after the residuals had returned to normal. During and after the swarm no long term residual changes were observed.

An inferred P-velocity scale is indicated on the right of Fig. 1. The assumption for this scale was that the residual increase was caused within the source volume of $r \approx 16$ km defined by the earthquakes. On this basis we estimate that the P velocity in the source region of the Matsushiro swarm decreased by approximately 20% about three years before the swarm. The entire pattern and magnitude of the anomaly is strikingly similar to premonitory velocity changes reported in other regions^{7,10,11}. This observation supports the notion that the Matsushiro earthquake swarm was not volcanic but tectonic in nature^{1,2}. The raising of temperatures above the Curie point and possible partial melting which may have taken place during the swarm in a volume with $r \approx 0.1$ km (ref. 12) could not have caused the decrease in velocity which, according to the residuals, occurred 3 yr before the swarm.

The precursor time in this case was approximately 1,260 d. With a cumulative magnitude of 6.3 this observation fits the precursor time magnitude curve^{7,11} with surprising accuracy. We conclude that if the precursor time interval curve and the P-wave residual anomaly at Matsushiro had been known in August 1965, when the swarm started with the occurrence of many small events (Fig. 1), a very strong case could have been made for the prediction of an imminent shock with magnitude near 6.

We propose that the routine monitoring of long term changes in the station residuals may be used as a tool for earthquake prediction at stations in tectonic areas. An important advantage of this approach is that the events to be predicted need not be preceded by seismicity in or near the future source regions.

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Stratospheric Observations from Nimbus 5

EXPERIMENTS using both infrared and microwave radiometers have been developed for the Nimbus series of satellites^{1,2}. Selective chopper radiometers (SCR) for Nimbus 4 and Nimbus 5 incorporate cells containing carbon dioxide gas to accomplish the narrow-band filtering, thereby achieving a very high effective spectral resolution—of the order of the width of the absorption lines themselves. By this means emission from levels in the atmosphere as high as 45 km can be selected. The first SCR on Nimbus 4, which was six channels in the 15 μm CO_2 band^{3,4}, has worked successfully for more than 3 yr; data from it have provided the first global maps of stratospheric temperature at these high levels⁵⁻⁷, and stratospheric warmings have been identified^{8,9}.

The SCR on Nimbus 5 is a more advanced instrument and possesses:

(1) It has a narrow field of view, equivalent to ~ 25 km resolution at the Earth's surface, which means that observations of areas which are cloud free or which have uniform cloud cover are more likely than with Nimbus 4.

(2) It has eight channels (groups A and B in Fig. 1) for temperature sounding in the 15 μm CO_2 band, from which three selectively chopped channels are derived (two on Nimbus 4) enabling better vertical resolution to be achieved.

(3) It has four channels for the identification and observation of cirrus cloud. Two of these (C1 and C2) are in the far infrared; C1 is sensitive to wavelengths greater than about 100 μm and C2 to a narrow band near 49 μm . These regions are chosen where water vapour absorbs strongly with approximately the same mean absorption coefficient in both regions. In clear conditions, observations of atmospheric emission in these spectral regions give an effective radiating temperature which is the same in both channels and representative of the upper troposphere. When high cloud is present, this equivalence no longer exists, because of the differing properties of ice particles in the two spectral regions. The difference in equivalent temperature therefore conveys information about high ice cloud.

The other two channels for observation of cirrus cloud are centred near 2.7 μm and 2.6 μm (D1 and D2 in Fig. 1) where CO_2 and water vapour have strong absorption bands. During the day, sunlight reflected from the atmosphere in these channels will be due to clouds in the upper part of the troposphere, so providing a further means of identification of high cloud.

(4) It has three channels in window regions (C4, D3 and D4 in Fig. 1). Atmospheric transparency is different in these three regions; also the variation of the Planck blackbody function with temperature is very different—at the shorter

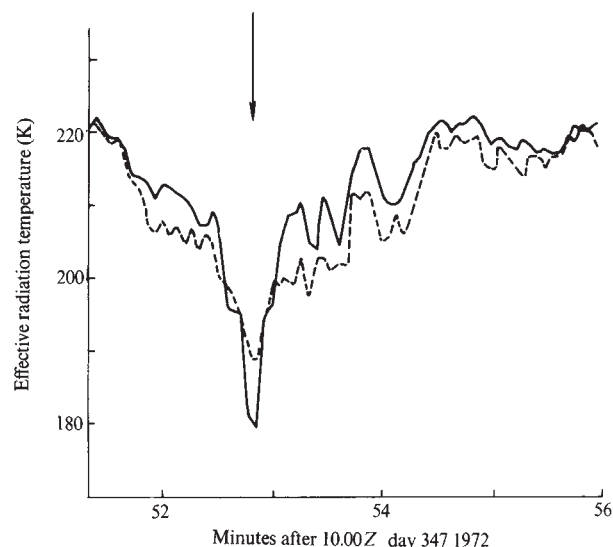


Fig. 2 Effective radiation temperature measured by channels C1 (—, $> 100 \mu\text{m}$) and C2 (---, $49 \mu\text{m}$) as the instrument passes over deep high cloud near the equator. At point marked by arrow, C3 ($18 \mu\text{m}$) and C4 ($11 \mu\text{m}$) both read 191 K.

wavelengths the variation is very steep. During the night, comparisons between them enable clear areas to be identified and sea surface temperature to be determined accurately. Further information about the structure of low cloud within the field of view is also provided.

(5) It has two channels for determination of atmospheric water vapour, C1 or C2 in a strongly absorbing region and C3 near 18 μm in a weaker region.

In Fig. 1 we show the spectral location of the various channels. A more complete description of the instrument is given elsewhere^{10,11}.

The prime objectives of the Nimbus 5 SCR are to carry out remote sounding of temperature, water vapour and cloud from the surface up to an altitude of about 45 km. Subsidiary measurements of cloud, water vapour and surface temperature are important in their own right but also enable tests to be made as to how well temperature retrievals can be obtained in the troposphere under a variety of conditions.

The Nimbus 5 SCR was switched on about 6 h after launch and has so far functioned perfectly. Initial analysis of the results has been confined to channels sounding high cloud, the plotting of global stratospheric maps and a comparison between Nimbus 4 and Nimbus 5 SCR data.

In Figs 2 and 3 we present observations over deep high cloud near the equator. The cloud in Fig. 2 is centred near 4°N , 190°E , and that in Fig. 3 is near 6°S , 180°E . From these figures we conclude:

(1) For the cases shown, away from the clouds, where the window channels indicate clear regions, the effective radiating temperatures in channels C1 and C2 are the same within ~ 1 K.

(2) Where the cloud is most opaque in Fig. 2, the measurements are consistent with the cloud emitting greater than 99% of blackbody radiation at the cloud top temperature at wavelengths of 11 μm , 18 μm and 49 μm , and about 94% of blackbody radiation at that temperature at wavelengths greater than 100 μm . The difference in effective radiating temperature, of 11 K at the centre of the cloud between channels C1 and C2, agrees reasonably well with the calculations of Houghton and Hunt¹², who predicted a difference in effective radiating temperature of up to 20 K for deep high cloud in a tropical atmosphere. The same effect though less pronounced can be seen in Fig. 3.

(3) In Fig. 2 where the cloud is less opaque, the effective temperature at C1 wavelengths is greater than that at C2. This is presumably because the cloud is more transparent at the longer wavelengths both because of the ratio of particle

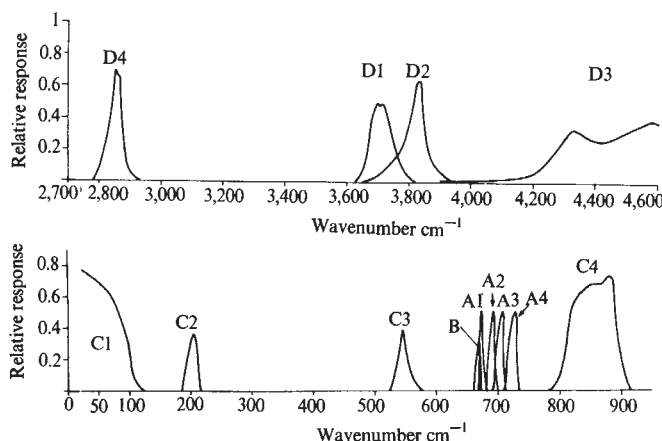


Fig. 1 Spectral response of the various channels of the Nimbus 5 SCR.

size to wavelength and also because of the behaviour of the absorption coefficient of ice. More radiation from lower in the atmosphere can therefore penetrate at C1 wavelengths than at C2. This effect of different transparency in the two spectral regions works in the opposite direction to the differing reflectivity mentioned in (2) above. Which effect is the greater depends on the number density and size of the particles in the cloud and the cloud thickness. For small particles the same effect was demonstrated by the calculations of Houghton and Hunt.

(4) The signal in channel D2 (near $2.6 \mu\text{m}$) is plotted in Fig. 3, expressed as an effective albedo. The variation of signal in this channel matches the emission signals in the long wavelength channels very well and the magnitude agrees well with predictions¹².

Our first look at the data shows that the combination of measurements of emission at long wavelengths and reflected sunlight at short wavelengths is potentially powerful in the investigation of the distribution and structure of high clouds.

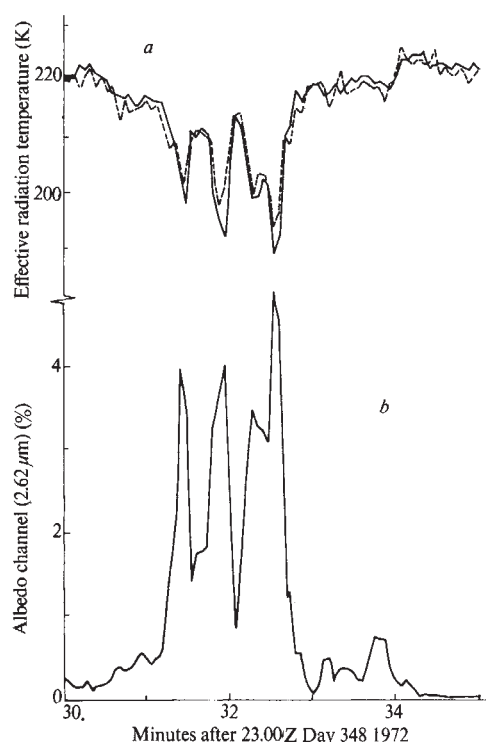


Fig. 3 *a*, Effective radiation temperature for channels C1 (—) and C2 (---). *b*, Measurements of reflected sunlight near $2.6 \mu\text{m}$ by channel D2 on the same occasion. Because of strong absorption in this spectral region, only sunlight reflected from very high cloud is detected by channel D2.

Maps of the emission measured by channel B12, in terms of equivalent temperature, which is approximately the mean atmospheric temperature averaged over a slab about 20 km thick centred at 45 km, are given in Fig. 4. The averaging function is similar to that for channel A of the Nimbus 4 SCR^{4,5}. On January 24 (Fig. 4*a*) the temperature field was disturbed, with cold centres over Northern Canada and Mongolia and a tongue of warm air extending from mid-latitudes over Europe to reach Northern Siberia. The disturbance subsequently increased in amplitude until the greatest zonal variation occurred on about January 28 (Fig. 4*b*). During this period the temperature over North-west Russia rose further to give a hot centre of 270 K, 18 K warmer than at the equator, while the cold centre over Asia moved eastward to merge with that over North America. This wave activity was accompanied by a rise of zonal mean temperature at high latitude; at 80°N for the same B12 channel the temperature

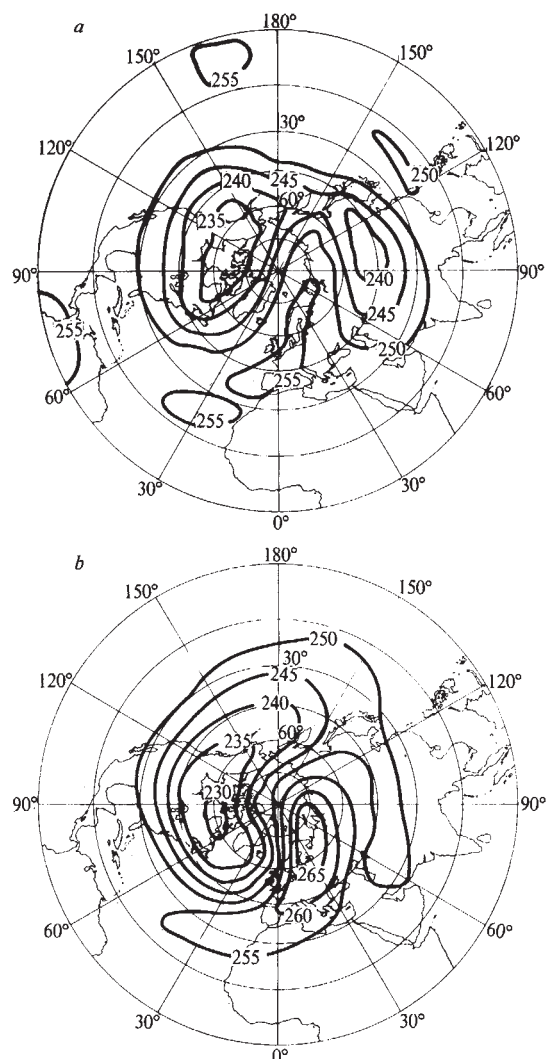


Fig. 4 Equivalent radiative temperature (K) measured by channel B12 for the northern hemisphere on *a*, January 24, 1973; *b*, January 28, 1973.

changed from 245 K on January 24 to a maximum of 254 K on January 30.

The progression of the warming was observed on all channels between A2, peaking at 110 mbar (16 km), and B12, peaking at 1.5 mbar (45 km). But the biggest change occurred at the channel centred at about 38 km, where the zonal mean temperature at 80°N , already relatively high for winter (230 K on January 24, compared with typical temperatures of 215 K for December 1972 and late February 1973), rose to 254 K on January 30. The dominance of the upper stratospheric temperature field by wavenumber two (two waves around the globe) on January 24 and wavenumber one on January 28 was followed by reversion to shorter wavelengths after January 30 with predominance of wavenumbers two and three.

Nimbus 4 and Nimbus 5 are in similar orbits, so direct comparison is possible between their SCRs. There seems to be no significant systematic difference between the highest channel of the Nimbus 4 SCR and a combination of Nimbus 5 channels arranged to match the Nimbus 4 channel.

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Anomalous Fading of Thermoluminescence in Mineral Samples

THE use of thermoluminescence (TL) for dating archaeological ceramics is well established¹. Recently we have been attempting to use similar techniques to date volcanic lava from geologically recent flows (5,000 to 50,000 yr old), by measuring the TL from the feldspars present. These included rhyolites from near Naples and basalts from Iceland and the Massif Central region of France; the latter were of particular interest because palaeomagnetic and potassium argon age measurements and related radiocarbon dates in the Chaine des Puys region have suggested a geomagnetic polarity excursion of the Earth's magnetic field within the past 50,000 yr (ref. 2). The basalts contained the plagioclase feldspars labradorite, andesine and bytownite, and the rhyolites contained the alkali feldspar sanidine. All of the TL ages obtained were significantly lower than the accepted ages of the lava flows, some by an order of magnitude.

The reason for this discrepancy is a loss of charge carriers from traps which contribute to the TL in the 350–450° C region of the glow curve. It is commonly assumed in TL dating, and expected on theoretical grounds, that at ordinary temperatures the lifetime of carriers in such traps is of the order of 10⁵ yr and upwards³. This loss is termed "anomalous fading" and its occurrence has been directly demonstrated in the laboratory for a variety of feldspars. Using the TL apparatus described by Aitken and Fleming³, and a ⁹⁰Sr/⁹⁰Y beta source for

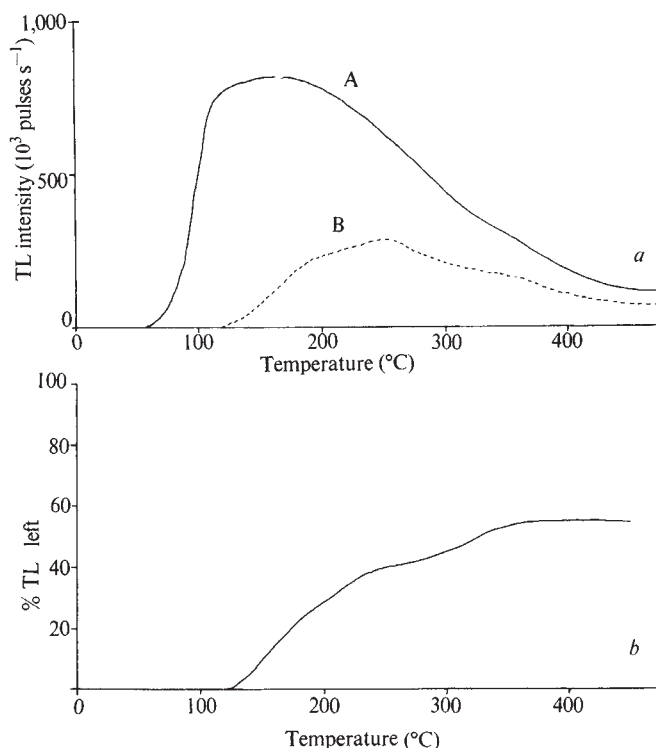


Fig. 1 a, TL glow curves for Massif Central basalt obtained immediately after irradiation (A) and after storing for 3 d at room temperature (B). The heating rate used was 6° C s⁻¹. b, TL intensity ratio curve derived from Fig. 1a. The ordinate represents the % TL left after storage for 3 d.

irradiation, each sample was put through the following procedure: (1) irradiate; (2) store in darkness at room temperature; (3) measure TL; (4) irradiate; (5) measure TL immediately. A check was made that there was no change in sensitivity in any of the samples used. In Fig. 1a I show the TL glow curves obtained for a basalt lava sample from the Massif Central (laboratory reference 132a1). The intensity ratio of the delayed glow curve to the immediate one is shown in Fig. 1b; there is a 45% loss of TL at the 400° C ordinate after storage for 3 d at room temperature. The behaviour of other lava samples followed this pattern. In Fig. 2a similar glow curves are shown for a sample of Norwegian alpha quartz and the ratio plot (Fig. 2b) shows no loss above the 250° C glow curve ordinate; the profile of the curve is that expected on account of the thermal emptying of the shallower traps only. Quartz is a material widely used in archaeological dating with satisfactory results⁴.

Table 1 Room Temperature Fading of Minerals

Mineral	Temperature ordinate (°C)	TL lost (%)	Storage time
Sanidine	300	25	4 h
Fluorapatite	400	40	15 h
Labradorite	350	40	15 h
Andesine	350	16	16 h
Zircon	350	16	17 h
Bytownite	350	10	8 d
Quartz	Above 350	0 ± 5	2 yr
Limestone	370	0 ± 5	2 months

Various feldspar separates, limestone, fluorapatite and zircon were also examined and the results for the samples showing the most acute fading are summarized in Table 1. Zircon and fluorapatite were included because their use for TL dating has been proposed⁵. Within experimental error the high temperature peaks in quartz and limestone do not show anomalous fading. About twenty different feldspar samples were studied; in five the fading was less than 5% after 4 weeks

storage, and in the remainder the behaviour was intermediate between this and the fading of the four feldspar samples quoted in Table 1. But failure to observe fading in a short term experiment does not exclude longer term fading. More detailed experiments on the samples in Table 1 indicate that there is a rapid initial fading followed by a much slower loss of TL with time. The shape of the decay curve does not, however, conform to any simple time dependence. A typical decay curve for fluorapatite is shown in Fig. 3.

Table 2 Effect of Temperature on Fading of 270 °C Peak in Fluorapatite

Storage temperature (K)	TL lost (%)	Storage time (h)
77	22	2
173	30	3
290	35	2
373	43	2

The effect of fading of the temperature at which the sample was stored during the delay period was examined. Storage at 255, 173 and 77 K gives decay rates which are slower at the lower temperatures (see Table 2) indicating some temperature dependence. So it is not strictly correct to describe the process as "non-thermal" as early work suggested⁶. Similar apparently "non-thermal" TL loss has been reported recently for lunar material⁷.

The fading does not seem to be related to surface effects as the fading rates 1–8, 50–100, 200–500 μm grains and also for a thin (300 μm) slice of the same material (fluorapatite) gave the same fading rates. The fading rate seems to be independent of the type of irradiation unless this is by alpha particles; an orthoclase feldspar (laboratory reference Z1) exhibited no detectable difference in rate after irradiation by

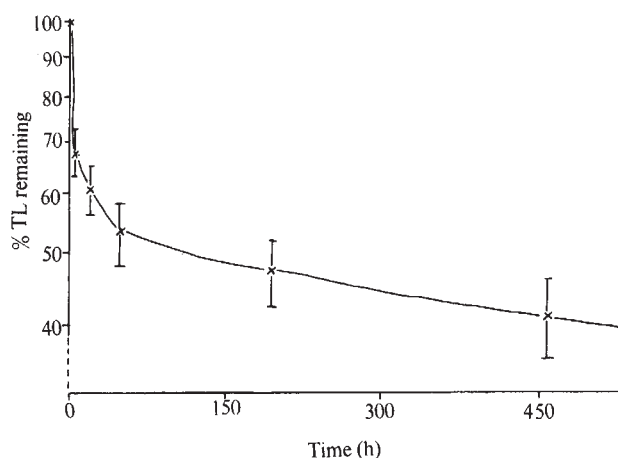


Fig. 3 Room temperature fading in fluorapatite. The ordinate, on a logarithmic scale, indicates the % TL remaining at the 350° C glow curve ordinate after storage for t h.

β particles, ultraviolet radiation (medium pressure Hg lamp) or γ rays (^{60}Co), but when ^{242}Cm alpha particles were used the loss at the 350° C ordinate after 100 h storage was 10% greater. The mechanism for the fading is now being investigated.

Use of research facilities provided by the Nuffield Foundation and an NERC studentship are acknowledged. I thank Dr F. B. Atkins (University Museum, Oxford) for supplying many of the samples, Dr M. J. Aitken for supervision and J. C. Aldred for discussions.

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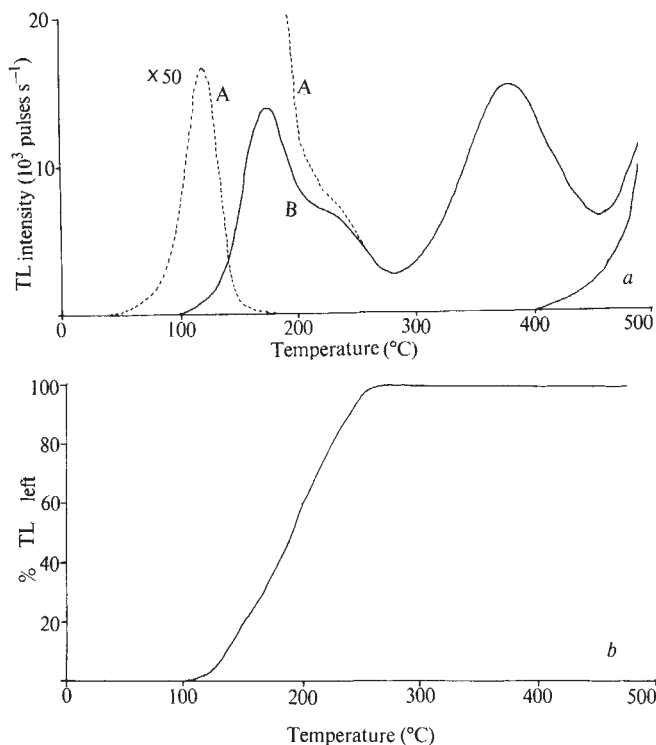


Fig. 2 *a*, TL glow curves for Norwegian alpha quartz obtained immediately after irradiation (A) and after storing for 3 d at room temperature (B). The heating rate used was 6° C s⁻¹. *b*, TL intensity ratio curve derived from Fig. 2*a*. The ordinate represents the % TL left after storage for 3 d.

Encounters of the Earth with Comets

THE proposal by Urey¹ that tektites may originate through Earth-comet collisions has recently been extended to suggest that the energy released may be sufficient to produce periods of intense geological activity². But the hypothesis is crucially dependent on the picture adopted for the structure of comets, and Urey assumes that the fundamental permanent heart-and-soul of a comet is a solid nucleus of kilometer size, with activity of the comet resulting from solar radiation and possibly interaction with the solar wind. If that were so, such an object impacting the Earth would not produce essentially different effects from those by a meteorite or asteroid of comparable mass.

In spite of the publicity devoted to the icy nucleus model, observations of comets make it clear that the hypothesis is untenable. These considerations have recently been reviewed in detail³, but it may be worth mentioning again some of the more inescapable instances. Comet 1927 IV remained visible out to 11.5 a.u., where solar heating would be negligible, and an object only kilometres in diameter would not be detectable at such distance. Comets do not appear as point-sources but expand up and grow fainter, merging with the background sky and vanishing through excessive diffuseness of their light. Again Comet 1729 had perihelion distance of more than 4 a.u. yet was visible to the unaided eye, and Comet Humason (1962 VIII) remained far outside the orbit of Mars yet developed a splendid tail. On the other hand, Ikeya-Seki (1965 VIII) developed a negligible tail when inside the orbit of Mercury. This difficulty was dealt with *ad hoc* at the time by claiming that the comet was "worn out", without explaining how this could be known for a freshly discovered comet. But immediately after perihelion it produced a tail 20° long visible to the unaided eye, as was predicted on the dust swarm hypothesis.

Another telling consideration is that only about 60% of comets have shown signs of any nucleus, and even for these not at all times nor at every return. The angular sizes of some nuclei when measurable are far too large to correspond to solid bodies, and though occasionally one may seem star-like to the eye there is no possibility of resolving an object of only kilometre size. The nucleus of 1882 II shortly after perihelion suddenly became a brilliant streak 200,000 km long, which then divided into five or six separate comets, resembling "a string of pearls". Yet another more recent observation unfavourable to the nucleus picture was Comet Bennett (1969i) which in H α was found to have an overall extent in excess of 10^{11} cm. Radiometric measures, interpreted as if relating to a nucleus, indicated a temperature of 700 to 800 K at about 0.55 a.u. from the Sun⁴: what sort of ice could this be? Yet again, during intense meteor showers (the debris of comets), there has been no instance of any meteorite reaching ground level in the shower orbit, decisive evidence that no large particles exist in comets. Finally, no feasible mechanism whereby such icy snowballs could form in the Solar System has been forthcoming.

On the other hand, from more than a century of observations before 1950, the structure inferred was that of vast swarms of widely separated meteoric particles, and this receives theoretical support from the accretion process for the formation of comets from interstellar dust. All the numerous accounts and interpretations by former skilled observers are still available, and it is only by ignoring this mass of evidence, not to mention modern observations, that the icy nucleus model can survive at all. Even the short period Comet d'Arrest has a coma 10^{10} cm or larger at times. But it is not likely that the actual limit to the particle distribution should be the mere optical limit, as the vast extent of Comet Bennett seen in H α would suggest.

With the particle structure for comets, the circumstances during an encounter with the Earth would be very different from those envisaged by Urey. First, the probability of encounter is much increased: on the nucleus basis, a direct hit would occur only about once every 50 m.y., but for a dust swarm 10^{10} , 10^{11} or even 10^{12} cm in linear dimensions, the Earth may on average pass through a comet more than once every million years. Other things are changed too, for if the relative speed is high, as it would be for long period comets, the Earth would only sweep up those particles directly in its path, with just a slight increase in effective radius from gravitation. The result would be a meteor shower over the forward hemisphere, probably on a most impressive scale; but the whole captured mass would only be of order 10^{15} g, and would correspond to a total entry energy of about 10^{27} to 10^{28} erg, not only three orders of magnitude less than on the nucleus picture, but spread over a time of order 1 d

and distributed through the high atmosphere, rather than an almost instantaneous meteoritic type of impact on the solid surface. But for short period comets of moderate eccentricity, the relative velocity can be low enough for an accretion stream to form behind the Earth by gravitational focusing, and then, in addition to meteors on the forward hemisphere, a captured jet of far denser heated material would fall to the Earth through the high atmosphere, and could by these means shower tektites onto comparatively small localities⁵. Although short period comets are generally smaller than long period ones, the amount of captured material could be of the same order because of the lower relative speed, and if only 0.1% were refractory material going to form tektites, this could still mean a fall of about 10^{12} g.

The same general kind of accretion process could also be initiated for the Earth by a meteoritic impact sufficiently energetic to remove the whole atmosphere above the general area of impact, thereby enabling material to be projected into orbits carrying it halfway round the Earth, again to be focused into a stream above the atmosphere by the accretion mechanism⁶. On either process, cometary or meteoritic, the resulting downward jet could persist for a period measured in hours, depending, in the cometary case, on the circumstances of passage through it, during which time the rotation of the Earth would spread the shower in longitude. This mechanism might well account even for the systematic differences in tektites with longitude claimed to have been established in the australite and indochinite fields.

Thus on the nucleus hypothesis, cometic collisions with the Earth would probably be too rare for possibly eight different tektite fields to have formed during the past 50 m.y., though whatever the details of the mechanism it could not be essentially different from that of the impact of a meteorite of comparable mass. In either case, for a mass of 10^{18} g, the energy could be 10^{30} to 10^{31} erg, as maintained by Urey, and would certainly be enough to produce worldwide devastation, though any detailed mechanism whereby objects resembling tektites would result in such a cataclysm has not been put forward. On the other hand, with the dust swarm picture, encounters with the Earth would be far more frequent, but only intense meteoric phenomena could occur for long period comets, with no serious consequences at ground level, unless indeed increased rainfall were stimulated thereby for a time, after the manner suggested for known meteor showers by Bowen⁷. But for short period comets there would be the possibility of formation of tektites by means of the accretion mechanism, and for this process the frequency of occurrence would accord with the number and ages of the known tektite fields.

Also, on the meteoritic or cometary nucleus impact hypothesis, tektites should be present on the other terrestrial planets and the Moon. But on the dust swarm cometary encounter hypothesis, tektites should be rarer on Venus than on the Earth, because of its smaller mass and higher orbital speed, rarer still on Mars and probably absent altogether from Mercury and the Moon⁵, though it may not be possible to verify these conclusions directly for some time.

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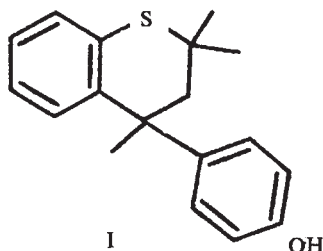
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Clathration as a Practical Method for Handling Dimethylmercury

THE interest in dimethylmercury in connexion with studies of environmental pollution prompts us to report a convenient and comparatively safe method for handling this volatile and extremely toxic compound. We have found that dimethylmercury may be stored, until ready for release, in the form of an inclusion compound, the organometallic guest being accommodated in the relatively large, approximately hour-glass shaped, cavity^{1,2} formed by the clathrate³ host, 4-*p*-hydroxy-



phenyl-2,2,4-trimethylthiochroman (Structure I). This represents the first successful attempt to prepare a stable inclusion compound containing dimethylmercury, although diethylmercury and longer chain mercury dialkyls have been reported⁴ to form inclusion compounds with urea; diethylmercury has also been included⁵ in the tri-*o*-thymotide channel structure.

The highly crystalline adduct, prepared by recrystallization of unsolvated³ (Structure I) from neat liquid dimethylmercury (cation), is found by NMR analysis to have a molecular ratio of host to guest of 6:1 (microanalysis requires 10.35% Hg; found 10.42% Hg). This host-to-guest ratio corresponds to single occupancy¹⁻³ of the clathrate voids.

The crystals suffer no detectable loss of guest (NMR analysis) even when pumped for several days under vacuum, the closed nature of the clathrate cage³ preventing escape of dimethylmercury. Grinding the crystals does, however, liberate sufficient guest to be detectable by mass spectrometry. Thus when crystals of the adduct in an evacuated flask attached to the inlet of a mass spectrometer are finely ground by using a magnet to agitate a small steel ball in the flask, the mass spectrum of dimethylmercury is observed. The minimal interference found from the spectrum of the host makes this an attractive method for obtaining mass spectra of guest molecules in clathrates.

The dimethylmercury 4-*p*-hydroxyphenyl-2,2,4-trimethylthiochroman clathrate is very convenient for preparing solutions of known concentration in dimethylmercury, pre-weighed quantities of the adduct merely being dissolved in the appropriate solvent.

Controlled release of organometallic guests from Structure I and other host lattices promises to be of considerable value in, for example, organic synthesis—especially where guest materials are difficult, or hazardous, to handle in the free state.

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Inhibitory Effect of Potent Interferon Preparations on the Regeneration of Mouse Liver after Partial Hepatectomy

INTERFERON exhibits a marked antitumour effect in mice inoculated with allogeneic or syngeneic transplantable tumours¹⁻³, but comparable interferon preparations did not affect the growth or development of newborn mice⁴. It is important from both a theoretical and a practical point of view to determine whether interferon can inhibit normal cell division in the animal. It has been shown that interferon preparations inhibited the multiplication of normal adult allogeneic spleen cells and syngeneic bone marrow cells injected into heavily X-irradiated mice⁵. Jahiel and his co-workers demonstrated that three interferon inducers, Newcastle disease virus (NDV), polyinosinicpolycytidylic acid and statolon, inhibited the mitotic response of liver cells after partial hepatectomy⁶, but that administration of interferon itself did not inhibit this response⁷. Now that potent and relatively purified mouse interferon preparations are available, we have used this experimental system, and report here a marked inhibition by interferon of liver regeneration after partial hepatectomy.

Three-month-old male Ajax mice were subjected to partial hepatectomy⁸. By determining the mean weight of the $\frac{2}{3}$ of liver removed, one can estimate the weight of the residual $\frac{1}{3}$ of liver and therefore also estimate the total RNA and DNA of the residual liver⁹. Two hours after hepatectomy and at intervals thereafter, mice were injected with an interferon preparation, mock interferon or left untreated. Mouse interferon was prepared from mouse sarcoma C-243 cells⁹ inoculated with NDV. The interferon preparation was concentrated and purified by ammonium sulphate fractionation and its activity assayed on L cells inoculated with vesicular stomatitis virus². Omitting the interferon inducer NDV, mock interferon was prepared, concentrated and purified in a manner identical to that used in the preparation of interferon. The time and the amount of interferon inoculated are presented in the legend of Table 1. (One unit of interferon as expressed in the text is the equivalent of 4 mouse reference units.) Forty-eight hours after hepatectomy, mice were injected with 20 μ Ci of ³H-thymidine (CEA, France) and were killed 1 h thereafter. Liver weight at 48 h is not a reliable criterion for an inhibitory effect on cell division because of varying degrees of steatosis⁸, so the criteria of regeneration were: total RNA and DNA; specific activity of DNA; and the number of labelled cells (autoradiography) on microscopic examination. Determination of RNA and DNA was based on the technique of Schmidt and Thannhauser as modified by Moulé¹⁰.

Repeated injections of partially hepatectomized mice with potent interferon preparations did not result in any increased postoperative mortality. Two experimental findings indicated that treatment of mice with interferon resulted in a marked inhibition of the synthesis of both total RNA and DNA. (1) The total amount of RNA and DNA present in the livers of control mice had increased at 48 h after operation, whereas the amount of RNA and DNA present in the livers of mice treated with interferon did not increase (comparison of the mean values at 0 h and 48 h: Table 1). (2) After a pulse of 1 h with ³H-thymidine the specific activity of DNA of the livers of control mice was much higher than that of mice treated with interferon (Table 1). (The finding that the amount of radioactivity present in the acid-soluble fraction was virtually the same for both control and interferon treated mice indicates that the block was in synthesis of DNA and not in precursor incorporation.) Synthesis of RNA precedes

Table 1 Inhibitory Effect of Interferon on the Regeneration of Mouse Liver after Partial Hepatectomy*

Experiment No.	Group	No. of mice	Total RNA (μg phosphorus RNA)		Total DNA (μg phosphorus DNA)		Specific activity DNA 48 h (d.p.m. μg^{-1} phosphorus DNA)	Autoradiography† (No. labelled cells per 1,000 cells per mouse)
			0 h	+48 h	0 h	+48 h		
1	Control preparation	14	250	380	60	80	2,390	135
	Interferon	14	250	246	60	60	220	15
			+ ± 13		+ ± 3.8		+ ± 230	
			+ ± 10		+ ± 3.3		+ ± 49	
2	Non-treated	11	Not tested		Not tested		5,990	90
	Interferon	15					1,527	15
							+ ± 994	
							+ ± 243	
							+ ± 19	
							+ ± 4	

Experiment 1: 3.6×10^6 units of interferon (specific activity 5×10^6 U mg^{-1} protein) in 0.2 ml were inoculated i.p. per mouse +2, +12, +21, +28, +35 h after hepatectomy. Experiment 2: 6.4×10^5 units of interferon (specific activity 10^6 U mg protein) in 0.2 ml were inoculated i.p. per mouse +2, +12, +22, +30 h after hepatectomy.

* The figures indicate mean value $\pm$ s.e.

† 2,000–3,000 cells counted per mouse.

‡ $P < 0.01$.

DNA synthesis in the regenerating liver⁸, so it is possible that the inhibitory effect of interferon on DNA synthesis is a secondary effect.

Decreased DNA synthesis itself may result from: (a) fewer liver cells in interferon treated mice synthesizing DNA; (b) the same number of liver cells in control and interferon treated mice synthesizing DNA, but the rate of DNA synthesis per cell being decreased in interferon treated mice.

The results of autoradiography indicated that fewer liver cells were labelled in mice treated with interferon than in controls (Table 1). Although grossly the extent of labelling of some cells seemed similar in both groups, we cannot exclude the possibility that differences in the amount of labelling per cell exist between control and interferon treated mice.

Interferon thus not only inhibits the growth of tumours in mice¹⁻³, the multiplication of tumour^{11,12} and normal cells *in vitro*¹³⁻¹⁶ but also inhibits the division of normal cells *in vivo* in some experimental conditions. Work is in progress to determine whether comparable interferon preparations can also inhibit normal cell division under less traumatic conditions than obtain after partial hepatectomy.

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Cannabinoid Phenotypes in *Cannabis sativa*

It has been suggested that "drug" strains and "non-drug" strains of *Cannabis sativa* L. comprise two comprehensive groups^{1,2}, which can be identified on the basis of their relative content of two of the principal "cannabinoids". Drug strains have been thought to contain an excess, usually substantial, of (–)- Δ^9 -trans-tetrahydrocannabinol (Δ^9 -THC) in comparison with the amount of cannabidiol (CBD), including carboxylate forms of both compounds, and non-drug strains have been held to have the reverse ratio. The former compound is considered psychotomimetic (psychosis-imitating), whereas the latter is not³. In examining the above cannabinoid ratio to decide in which phenotypic group a strain belongs, some investigators² add the amount of cannabinol (CBN) to the amount of THC. The former seems to be an oxidation product of Δ^9 -THC (ref. 4) and is not considered to be psychoactive.

Investigators⁵⁻⁷ have reported that in some samples of the high-THC category of plant, there is a complete absence of CBD. Turner and Hadley⁷ note that in most gas-liquid chromatography (GLC) systems, two additional cannabinoids, cannabichromene (CBC) and cannabivarin, cannot be effectively separated from CBD. As some samples have small amounts of CBC (but no CBD) in combination with large amounts of THC, there is a possibility that previous reports in the literature have mistaken CBD for CBC in some samples of the high-THC category of plant. In our own GLC system, we are confident that we can distinguish CBD. Although we examined many samples of the high-THC category of plant, none were completely without CBD.

Our principal aim was to verify the existence of the two basic categories of plant, one rich and the other very low in Δ^9 -THC. To examine the general applicability of these phenotypic categories, and to see if other patterns existed, we examined 350 stocks of *Cannabis* for their content of the major cannabinoids, Δ^9 -THC, CBD, and CBN.

Diverse strains of *Cannabis* were acquired from a variety of sources from about fifty countries, and grown out of doors in Ottawa during the summer of 1971. Three males and three females were collected at maturity (six vegetative

plants were collected where a particular stock failed to flower before frost), males maturing a month before females. "Manicured" marijuana was prepared by sieving the flowers and leaves through a screen, and samples were analysed by GLC. An internal standard and reference samples of the cannabinoids were used to characterize a sample of hashish, which in turn was used as an external standard for the samples being analysed. Detailed results and methodology will be published elsewhere.

The strains of *Cannabis* we examined were assigned to three large modally distinct groups with respect to their cannabinoid content. A plot of THC content against CBD content for female plants (Fig. 1) reveals these groups. Mean absolute concentrations of Δ^9 -THC and CBD are indicated for these three "types" in Fig. 2.

In type I, both male and female plants possessed large amounts of Δ^9 -THC and very limited amounts of CBD. For classification purposes, type I was defined as having more than 0.3% THC and less than 0.5% CBD. Such potent varieties usually originated from countries south of latitude 30° N. Many strains probably conforming to this type failed to come into flower in the relatively short growing season of Ottawa.

In types II and III, large amounts of CBD (more than 0.5%) were usually present. Such varieties usually originated from countries north of latitude 30° N. Female plants possessed substantially higher contents of cannabinoids than did the males. Most of these strains completed their life cycle in the Ottawa climate. Type III plants contained very little Δ^9 -THC (less than 0.3%), and were not considered psychotomimetic. Type II strains were defined as having high mean contents of both CBD (more than 0.5%) and THC (more than 0.3%). This arbitrary classification distinguishes high CBD strains which are non-psychotomimetic from high CBD strains in which the females at least can be considered psychotomimetic. Type II strains were frequently cultivated for the production of fibre, oil, or seed. These strains varied considerably in their ratio of THC to CBD, and individuals of such varieties could not consistently be distinguished from type III on the basis of the ratio of THC to CBD. The existence of high THC levels in some strains conforming to the northern characteristics

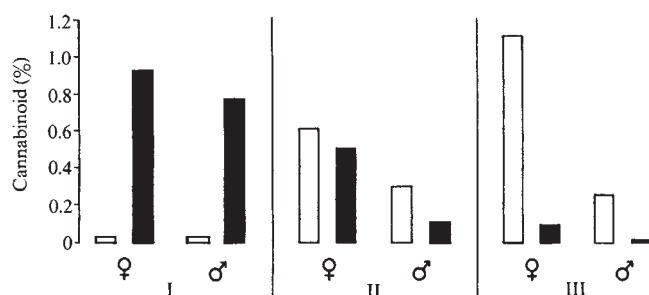


Fig. 2 Common patterns of cannabinoid association. Numerals refer to phenotype designations. □, CBD; ■, THC. Height of bars is proportional to mean values for the strains examined which conformed to the "type".

(high CBD levels, marked differences in content of males and females, and relatively early maturation) may reflect hybridization with type I strains introduced by plant breeders and dealers in cannabis drugs.

CBN was rarely found. A second isomer of THC, $(-)\Delta^8$ -trans-tetrahydrocannabinol, was consistently present in very limited quantity, always less than 0.1% of the weight of the prepared samples.

Yamauchi *et al.*⁸ have reported that cannabigerol monomethyl ether (CBGM) was present in a sample of Japanese marijuana. In the strains we examined from northeastern Asia, all of the prepared samples consistently showed trace amounts (of the order of 0.05%) of a material whose retention time matched that of CBGM.

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Immunosuppressive Properties of the Lymphocyte Chalone

EXPERIMENTAL evidence indicates that a number of cells are mitotically controlled by specific and endogenous negative feedback inhibitors of mitosis called "chalones"¹⁻³. Moorhead *et al.*⁴ were the first to apply this concept of a negative feedback inhibitor of mitosis to the lymphocyte system. They demonstrated that extracts of pig lymph node contained material which would inhibit the transformation of PHA-stimulated human lymphocytes in culture and the *in vitro* mitotic activity of lymphocytes derived from patients with lymphocytic leukaemia⁵. These observations have been confirmed and extended⁶⁻⁹. Because of the importance of lymphocyte transformation to the phenomenon of graft rejection, Garcia-Giralte *et al.*¹⁰ and Kiger *et al.*¹¹⁻¹³ demonstrated that extracts of lymphoid tissue could partially inhibit both graft-versus-host and allograft rejection in mice.

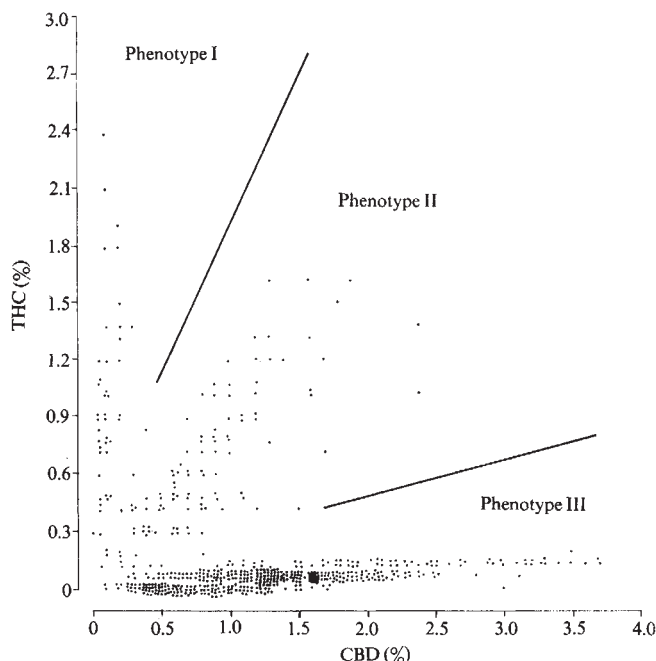


Fig. 1 Graph of THC content plotted against CBD content in female plants. Clustered points have been displaced slightly for clarity. A few individuals from colonies classified as phenotype II fall into range of phenotype III.

Here we describe the concentration and partial purification of lymphocyte chalone and its application to immunosuppression in both *in vitro* model systems and *in vivo* studies of mouse skin allograft rejection.

Table 1 Inhibition of Mixed MLC (Donors A and B) by Lymphocyte Chalone Concentrate

	C.p.m. per 10 ⁶ mononuclear cells		Average % inhibition
	Experiment 1	Experiment 2	
A cells alone	50	114	—
B cells alone	126	60	—
A and B cells	18,500	22,000	—
A and B + 100 µg	2,100	2,900	92
A and B + 75 µg	3,400	4,300	81
A and B + 50 µg	6,800	8,900	60

Acetone powders of calf thymus and spleen were prepared in the cold, extracted (10 ml g⁻¹) into water, allowed to stand overnight at 4° C, centrifuged and subjected to molecular sieving in the Amicon Diaflo system^{14,15}. Inhibitory activity against both PHA-stimulated transformation of lymphocytes in culture and against spontaneous mitotic uptake of ³H-thymidine by human lymphoblastic lymphocytes in culture (NCTC-37) was found concentrated in the molecular weight range 50,000 and 10,000 with most of the activity being found between 30,000 and 50,000 as previously reported⁸. This activity was apparently non-cytotoxic. The latter molecular weight range was then dialysed and lyophilized. Approximately 50 µg ml⁻¹ of the lyophilized, sieved materials from either spleen or thymus acetone powders would inhibit about 50% of the ³H-thymidine uptake by 500,000 human lymphocytes ml⁻¹ when stimulated by PHA in culture^{8,9}. The effects of 100, 75, and 50 µg ml⁻¹ of lymphocyte chalone concentrate from the spleen, upon the uptake of ³H-thymidine by 500,000 mononuclear cells ml⁻¹ (from two separate donors cultivated in "mixed lymphocyte culture" (MLC) in Medium 199 supplemented with 20% calf serum, glutamine, and 'Pen-Strep' (Gibco)) are shown in Table 1. These data indicate that 90% of the ³H-thymidine uptake during a 7 d incubation *in vitro* in MLC was inhibited by 100 µg ml⁻¹ of molecularly sieved and concentrated lymphocyte chalone activity from spleen. As little as 50 µg ml⁻¹ will inhibit over half of the total immunologically stimulated transformation of these human cells in culture. Similar results were obtained using extracts of thymus. This MLC incubation system has been helpful in predicting the intensity of subsequent clinical graft rejection¹⁶.

Table 2 Effect of Lymphocyte Chalone Extract upon the Inhibition of Transformation and Release of MIF from Human Lymphocytes

Thymus extract (µg ml ⁻¹)	% Thymidine	MIF activity (%)
0	0	67
5	10	58
10	18	50
15	25	42
20	33	36
25	45	10*
50	58	0*

* Statistically insignificant macrophage inhibition.

Using a new method for the determination of macrophage migration inhibitory factor (MIF), which is extremely sensitive and quite rapid¹⁷, we studied the effects of various concentrations of sieved concentrated lymphocyte chalone from spleen upon both the PHA-stimulated transformation of human lymphocytes in culture, as judged from the uptake of ³H-thymidine, and also the release of MIF activity into the supernatant of these cultures. These data are presented in Table 2 and clearly indicate that there was a parallel inhibition of both thymidine uptake and MIF release from trans-

forming lymphocytes with increasing amounts of lymphocyte chalone concentrate until, at 25 µg ml⁻¹, approximately 45% of the thymidine uptake was inhibited and no significant amount of MIF activity was released into the culture medium. Because of the considerable importance of MIF to the immunological defence mechanism of the body in terms of graft rejection¹⁸, these data, together with those described in Table 1, support the possibility of successful immunosuppression by lymphocyte chalone concentrate.

Table 3 The Survival of Skin Allografts in C57Bl/6 Mice from C3H Mice with and without Lymphocyte Chalone

	Untreated	Chalone	Control
No. of mice	12	12	10
Mean survival time (d)	10.5 ± 1	29 ± 2*	10.5 ± 1
Range (d)	9-12	27-31	10-12

Chalone administered at 5 mg d⁻¹ three times per week.

* Significantly different from untreated or control animals (*P* < 0.01).

Thirty-four male C57Bl/6 mice had skin allotransplantation from C3H mice in the usual fashion¹⁹. Twelve of these animals received 0.2 ml of 0.15 M NaCl intraperitoneally, twelve received 5 mg of lymphocyte chalone concentrate from the spleen per 0.2 ml of 0.15 M NaCl intraperitoneally, and ten animals received 5 mg of 50,000 to 30,000 molecular weight range fraction made as described above from calf muscle per 0.2 ml of 0.15 M NaCl. All three groups of animals were injected on the first day and then received further injections every other day (except Sundays) for 3 weeks. These results are summarized in Table 3. All grafts in the control and saline-treated animals were rejected by 12 d. The chalone-treated animals retained their grafts for about 29 d, with rejection occurring 8 to 10 d after cessation of chalone treatment. Thus, the survival of C3H mouse skin grafts on the chalone-treated C57Bl/6 mice was prolonged 2.5 times that of the control mice. Only nine doses of lymphocyte chalone were used per mouse in this study because of limitations in the amount of the partially purified sieved spleen extract available.

These data suggest, first, that lymphocyte chalone concentrate from spleen could inhibit the immunologically produced transformation of human lymphocytes in mixed lymphocyte culture and, second, that this chalone concentrate could inhibit the release of MIF from transformed human lymphocytes *in vitro*. This latter finding suggests that lymphocyte chalone concentrate might also have an ameliorative effect in limiting delayed-type hypersensitivity reactions *in vivo*. The *in vivo* demonstration of the inhibition of allograft rejection appears quite convincing quantitatively in spite of lack of knowledge as to the proper dose regimen and concentration of this lymphocyte chalone concentrate for these animals. All three of these experimental results suggest strongly that lymphocyte chalone from spleen possesses immunosuppressive properties that warrant further experimental attention.

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Growth of Pulmonary Alveolar Macrophages *in vitro*

THE mammalian pulmonary alveolar macrophage (PAM) plays a primary role in removing and detoxifying foreign materials reaching the terminal airways¹⁻⁴. The metabolic characteristics of PAMs associated with their function as detoxifying and clearing agents *in situ* have been the subject of recent study⁵⁻⁸, but the PAM remains a poorly studied cell type⁹. PAMs have been considered a specialized cell type incapable of survival *in vitro* for extended periods or of division in culture^{10,11}. In the lung, the PAM population is constantly being renewed¹²⁻¹⁵: cells leave the lung by migration into the blood^{16,17}, the lymphatic system^{9,18}, by cell breakdown and clearance by other PAMs¹⁹, or by mucociliary transport^{1,15,16,20}; and are renewed by migration of stem cells to the lung interstitium^{13,14,21}, by division of precursor cells in the interstitium^{22,23}, or by division of mature PAMs in the alveoli²⁴.

We report here that mammalian PAMs obtained by pulmonary lavage can be maintained *in vitro* in standardized conditions for long periods and can proliferate indefinitely when provided with factor(s) synthesized by a cell line of isologous peripheral lung tissue.

PAMs were obtained from young adult C57Bl mice. With the animals under pentobarbital anaesthesia the trachea was exposed and cannulated, and ten successive washings (each 0.75 ml) were performed with isotonic saline¹⁷. Cell suspensions were examined in a haemocytometer and any containing erythrocytes were discarded. The cells obtained from each mouse were pooled, centrifuged at 1,000 r.p.m., and seeded at a concentration of 5×10^3 cells per culture in 35-mm plastic culture dishes (Falcon Plastics) containing 1 ml of medium. After 30 min of incubation non-adherent cells were removed with two changes of medium. All cultures were incubated at 37° C in a humidified atmosphere of 5% CO₂ in air. The medium was replaced twice a week.

The medium used in these experiments was Ham's F-12 supplemented with 15% foetal calf serum and penicillin-streptomycin at final concentrations of 50 U-50 µg per ml

(Microbiological Associates). This medium will be referred to as F-12 medium.

F-12 medium exposed to confluent cell cultures for 3-4 d was collected, passed through a 'Nucleopore' membrane (General Electric Co.) of pore size 0.45 µm and used for PAM cultures after adding an equal amount of fresh F-12 medium and 10% (final volume) foetal calf serum. This medium will be referred to as conditioned medium (CM).

Three types of CM were prepared. CM121370 was prepared from cultures of mouse cell line 121370, a rapidly proliferating long-lived line derived in this laboratory from adult C57Bl peripheral lung tissue²⁵. CMWI38 was prepared from cultures of WI38 human foetal lung fibroblasts²⁶. CML-929 was prepared from cultures of mouse L fibroblasts, clone 929, originating from a mouse subepidermal tumour²⁷. These cell lines are maintained in F-12 medium.

Cell suspensions obtained by pulmonary lavage were quite homogeneous^{3,13,17}. Differential counts of May-Grünwald Giemsa stained smears indicated 96%-97% of the cells were macrophages, <3% lymphocytes and <1% monocytes. More than 96% excluded trypan blue²⁸. This was operationally considered a pure PAM population^{3,17,29}, although identification of individual cells in unstained smears and early cultures was difficult (Fig. 1a). When incubated for 30 min in a 0.1% 'Zymosan' suspension more than 95% of the non-lymphocytes were phagocytic, although the amount of 'Zymosan' associated with each cell varied considerably³.

PAM cultures maintained in F-12 medium for periods of up to 16 weeks presented a uniform appearance characteristic of non-proliferating cells: the cells remained rounded-up, mitotic figures were never observed, and cell number and total cell protein (Fig. 2) did not increase. These cells phagocytosed 'Zymosan' particles for at least 6 weeks. In cultures initially given CM121370 mitotic figures were first observed within 24-36 h, cells spread out, became vacuolated, motile, and proliferated at a steady rate. This proliferation was steady and sustained. The population did not respond uniformly:

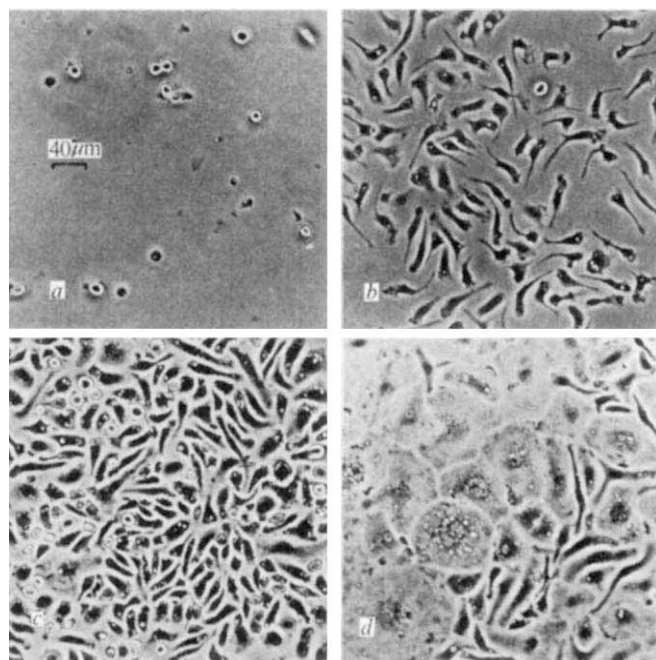


Fig. 1 Morphology of PAM cultures exposed to CM121370. Phase-contrast micrographs of cells in culture ($\times 112.5$). a, A culture 24 h after initiation showing the first division figures. b, A low density culture 14 d after initiation. c, The same culture 35 d after initiation. d, A high density tertiary PAM culture: these cells have been in culture 15 weeks and have been passaged twice with trypsin-citrate.

in the same culture some cells remained rounded-up, some became stellate, and others polygonal (Fig. 1b and c). All these cells phagocytosed 'Zymosan' particles. Cultures maintained in F-12 medium for 3 weeks and switched to CM121370 responded as just described and proliferated at a rate comparable to parallel cultures given CM121370 throughout.

Cells cultured in CMWI38 for 3 weeks did not respond. The cells were phagocytic, but neither division figures nor accumulation of protein were observed. These cultures were morphologically indistinguishable from parallel cultures in F-12 medium. When these cells were switched to CM121370 division figures were seen within 48 h and cellular protein accumulated at a rate comparable to that of parallel cultures in CM121370. Cultures in CML-929 died within 1 week. Parallel cultures in F-12 medium remained viable for at least 4 weeks and proliferated when exposed to CM121370. Dense cultures of PAMs have been passaged using either trypsin (0.5%) or 'Pronase' (0.025%) in citrate buffer at pH 7.4³⁰. Proliferating tertiary cultures are shown in Fig. 1d. These cells phagocytosed 'Zymosan' particles despite their altered morphology and proliferated when supplied with CM121370. When given F-12 medium only, these cultures stopped proliferating.

We have partially characterized the factor(s) present in CM121370 responsible for the effects observed in PAM cultures. The factor(s) are stable to freezing and thawing; non-dialysable, and are not inactivated by trypsin (Difco 1 : 250), collagenase (Worthington CLS), or 'Pronase' (Calbiochem B grade), at 100 $\mu\text{g ml}^{-1}$ in citrate buffer at room temperature for 6 h. The factor(s) pass through a protein retentive Amicon centriflow membrane (Amicon CF-50) with a molecular weight cut-off of 50,000. Low-molecular-weight growth and differentiation factors³¹ and cofactors³² have been demonstrated in other systems. Phytohaemagglutinin^{33,34} and pokeweed mitogen³⁵ are low-molecular-weight plant mucoproteins which induce mitosis in cultures of macrophages. PAMs have previously been observed to divide infrequently, if at all, *in vitro*^{11,12,34,35}. It has seemed that the PAM might be a post-mitotic terminal cell³⁶ which, in certain conditions, might be maintained in a non-dividing state. Our results indicate that PAMs may require specific substances for proliferation: only CM121370, containing factor(s) synthesized by cultures of isologous peripheral lung tissue, stimulated PAMs to divide. CMWI38 maintained the PAMs, which could subsequently be stimulated to divide on exposure to CM121370, while CML-929 was toxic. We have not identified the toxic factor(s) in CML-929: two possibilities are tissue-specific factors or the tumorous origin of L cells. Additional work indicates that proliferation of PAM cultures is co-existent with the specialized function of phagocytosis.

This work is in agreement with reports indicating a continuing need for "inducing substances" for continued proliferation in cultures of rat marrow macrophages³⁷ and mouse peritoneal macrophages^{35,38}. Cultures switched from CM121370 to F-12 medium cease to accumulate cellular protein (Fig. 2) and after a few weeks begin to round up and assume the morphology of a culture maintained in F-12 medium: this phenomenon supports the hypothesis that a cell's *in vitro* shape and activity can be thought of as an interaction of a particular cell with a particular environment³⁹.

Recently Evans *et al.*²⁴ showed that rat PAMs divide in alveolar spaces and terminal bronchioles after alveolar injury by exposure of the animal to NO_2 . This evidence and ours strongly suggest that the lung can respond to such injury by division of differentiated PAMs in the terminal airways. It is unclear whether this is a specific response to a demand for more PAMs or a more general injury response.

It is not known whether migration of stem cells to the lung or division in the lung interstitium and/or alveolus is the principal mechanism in the normal or pathological replacement of macrophages. Both mechanisms have been demonstrated, the former in peritoneal macrophages²¹, and the latter in

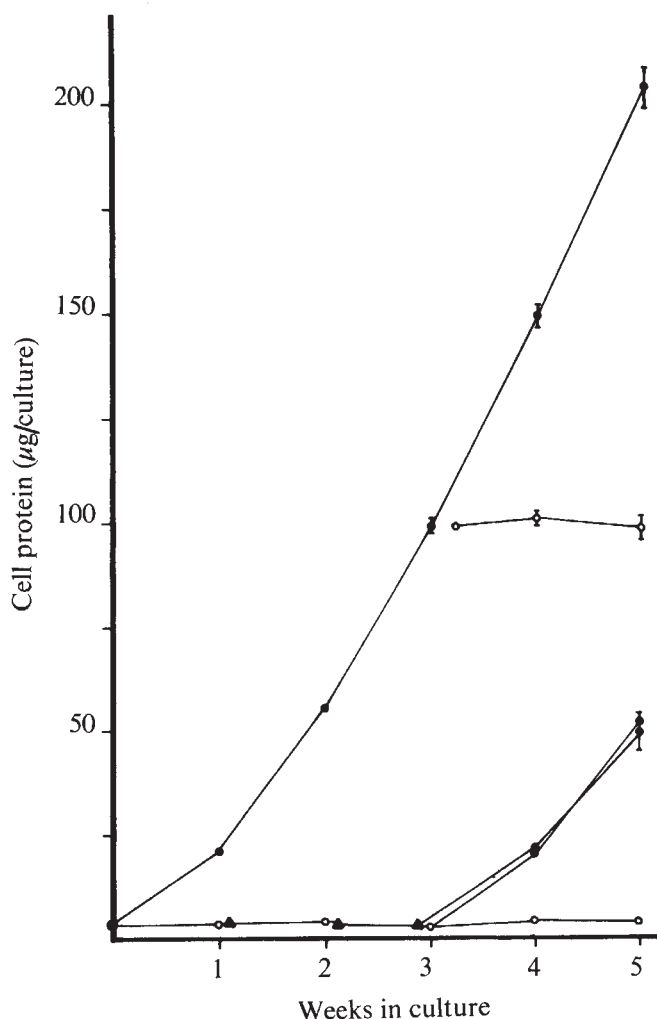


Fig. 2 Effect of medium composition on the proliferation of PAM cultures. Cell protein was determined by a modified Lowry method using albumin as standard. Values are means $\pm$ s.e. $\circ$, F-12 medium; $\bullet$, CM121370 medium; $\blacktriangle$, CMWI38 medium.

PAMs²⁴ and in liver macrophages⁴⁰. Our results demonstrate that both mechanisms may occur in the mammalian lung.

Further work is directed toward understanding changes in growth and function of stimulated PAM cultures with respect to the age of the donor animal, differing environmental conditions, and the nature of the stimulating factor(s).

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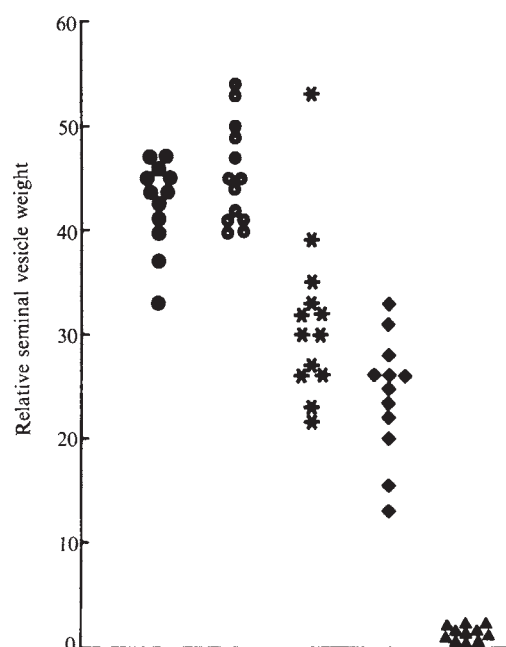


Fig. 1 Relative seminal vesicle weights of (C57Bl × CBA(T6)) F₁ hybrid mice, 3 months after the operation was performed on mice 3 weeks old. ●, Normal mice; ○, sham operated mice; ▲, castrated mice; *, transplant at the dorsal site; ◆, transplant at the snout site.

After 3 months the animals were killed to determine the appearance and histological structure of the graft and the weight of the seminal vesicles. Observations were also made in castrated, non-transplanted animals and sham operated control mice, in which the same operation was performed apart from ligating the spermatic cords and removing the testes.

The weights of the seminal vesicles were expressed as an arbitrary, convenient ratio of the weight of the vesicles to the body weight of the animal thus:

$$\text{Relative seminal vesicle weight} = \frac{\frac{1}{2} \text{ weight of both seminal vesicles (mg)}}{\text{body weight of mouse (g)}} \times 10$$

Following bilateral orchidectomy in adolescent animals, the seminal vesicles did not develop and in adults they atrophied. When testicular suspensions were implanted, however, development was restored, but to varying degrees according to the site employed (Fig. 1). The subcutaneous dorsal site was the most effective, relative seminal vesicle weights being nearly as great as those of controls 3 months after grafting.

Examination of the seminal vesicles revealed that those from castrated animals contained little or no secretion, whereas those from normal, sham operated and transplanted animals showed distension of the collecting spaces with secretory material.

The graft areas 3 months after transplantation appeared as well vascularized, light pink, localized swellings. The blood vessels were easily seen with the naked eye and were prominent in many cases. Histological study of these grafts showed that initially there was some round cell infiltration with proliferation of fibroblasts and occasional giant cell formation. Seminiferous tubules were atrophic in all cases and there was no evidence of spermatogenesis but interspersed within this tissue were small groups of larger cells containing granular cytoplasm which stained pinker with haematoxylin and eosin than the surrounding structures. These cells were indistinguishable from those of normal interstitial cells. Mitoses were not seen but the clumps seemed to become larger with the progression of time over the 3 month period studied. The largest

Transplantation of Interstitial Cells of the Testis

ATTEMPTS to transplant the testis have been made for many years but with little success. Difficulties with vascular anastomoses when whole organ transplantation was employed and the effects of immunological rejection have been the major problems^{1,2}. More encouraging results, however, have been reported following the grafting of separated components of the testes into intraocular sites in the rat³ and 'Millipore'-type chambers in the rabbit⁴.

Our experiments were devised to study the fate of homogenate suspensions of the testis when grafted into various sites in castrated inbred mice, and to assess their effects on primary and secondary sexual development.

Autotransplantation was performed in groups of (CBA(T6) × C57Bl) F₁ hybrid mice at the ages of 3 weeks and 3 months. Bilateral orchidectomy was carried out under ether anaesthesia through a mid-line vertical lower abdominal transperitoneal incision. Both testes were placed in a sterile Petri dish containing three to four drops of normal saline and cut up finely with scissors. The resulting thick suspension was aspirated into a brain-type cannula and then injected into localized areas in ear pinnae, under the skin of the back and snout and under the parietal peritoneum.

collections were found in the sites under the parietal peritoneum.

We have established that autotransplantation of free testis homogenates can be achieved in the mouse with survival of interstitial cells, good vascularization of the graft and near normal development of the seminal vesicles.

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Electron Microscope Autoradiography of Kidney after Administration of ^{210}Pb in Mice

WHEN mammals are exposed to lead, the metal is incorporated into various tissues and also excreted in urine and bile. Lead is considered to pass into urine not only by glomerular filtration but also by direct transport through the tubular epithelial cells¹. Histologically, tubular epithelial cells of lead poisoned kidney have been reported to have nuclear² and extranuclear inclusions or concretions^{3,4}, which are thought to contain lead. Biochemical examination of the kidney after administration of lead revealed that a considerable amount of lead was bound to mitochondrial and microsomal fractions⁵. Thus, the tubular epithelial cells of the kidney are understood not only to excrete lead into urine but also to deposit some to form inclusion bodies. The transportation of incorporated lead and the process of the formation of the inclusion body in the epithelial cells have, however, not yet been demonstrated.

We used electron microscopic autoradiography to demonstrate the precise localization of ^{210}Pb in some organelles in the tubular epithelial cells of the mouse kidney.

Male mice (dd strain; aged 12 weeks, body weight 35 g) were injected intraperitoneally with 0.5 ml of solution of RaD (400 μCi) in 0.1% acetic acid. The mice were killed 30 min after injection and the kidney was fixed with 4% glutaraldehyde buffered to pH 7.1 with sodium phosphate, and postfixed with 1% osmic acid. Small pieces of the tissue were dehydrated and embedded in 'Epon' mixture. Sections for electron microscopic autoradiography were placed on celloidine coated slides, stained with uranyl acetate and lead nitrate. The slides were dipped in Ilford L4 emulsion, and exposed for 70 d. RaD (specific activity 8.7 mCi mg^{-1}) purchased from the Radiochemical Centre was dissolved in 3 N nitric acid. The solution was neutralized with 3 N potassium hydroxide giving a white precipitate of lead hydroxide, which was redissolved in 0.1% acetic acid solution.

RaD contains ^{210}Pb , ^{210}Bi and ^{210}Po in radioactive equilibrium. α -Emission of ^{210}Po does not result in the appearance of silver grains in the emulsion and the energy of ^{210}Bi is too great to be trapped in silver halides. Most of the grains observed were, thus, related to ^{210}Pb .

Hexagonal silver grains in the renal medulla were principally associated with the tubules; there were few grains on

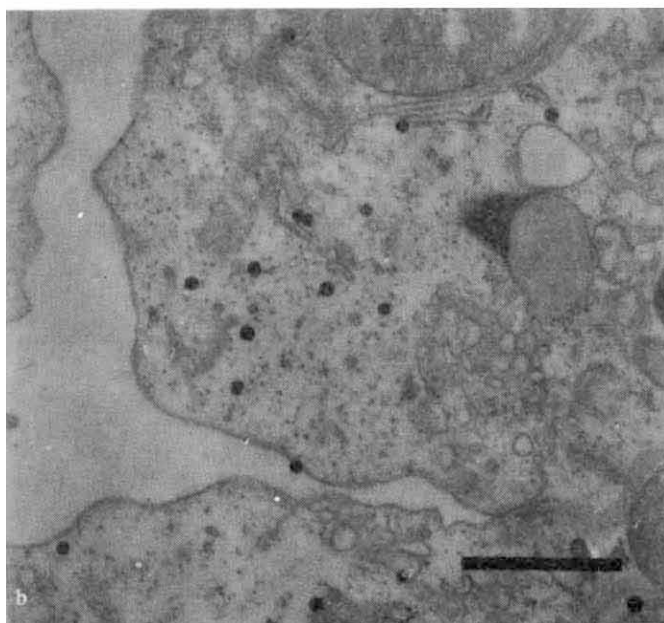
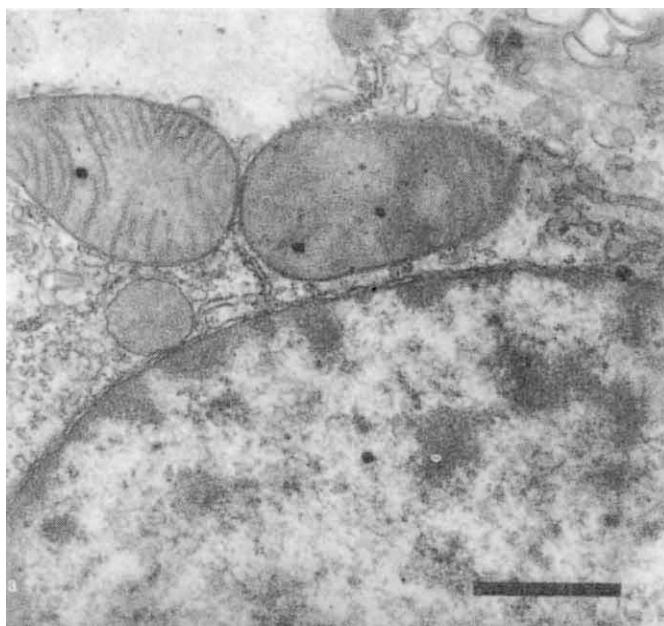


Fig. 1 a, Electron micrograph of an epithelial cell of the rat distal tubule. Silver grains are observed over nucleus, nuclear membrane and mitochondrial matrix. Intramitochondrial granules are also found, which are distinguished from silver grains. Bar=1 μm . b, Silver grains are distributed over the apical cytoplasm of a renal distal tubule cell. Most of grains are scattered on cytoplasm free of cytoplasmic membranes. Bar=1 μm .

the connective tissue and capillary endothelial cells. Counting the grains on 20 tubules showed that in the epithelial cells, more than half of the grains were found on mitochondria and about one third on the cytoplasm, half of which were associated with the cytoplasmic membranes. A few grains were found on the nuclei of the epithelial cells (Fig. 1a, b). These results indicate that lead is accumulated in the mitochondria and in the cytoplasm as soon as 30 min after its administration.

Biochemical investigations have shown that large amounts of radioactive lead are accumulated in the mitochondrial fraction of the kidney after intravenous⁶ or intraperitoneal administration⁵. Goyer⁷ reported that mitochondria isolated from rats after administration of lead had a decreased rate

of respiration and partially uncoupled oxidative phosphorylation. In the microsomal and the soluble fractions, radioactive lead is detectable 2 h after intraperitoneal administration⁵.

In the present study, grains were found on the various kinds of membrane and on the cytoplasm free of membranes. Thus, the cytoplasm as well as the membranes, seem to be involved in the incorporation and transport of lead. Few grains were found on the nuclei 30 min after administration. Choie⁸ found that nuclear inclusion bodies were formed in the renal proximal tubules 24 h after a single intraperitoneal injection of lead in the rat, which is consistent with the limited inclusion of lead into the nuclei found in this shorter study.

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Inherited Differences in Intensity of Alcohol Withdrawal Reactions in Mice

It is not known whether alcoholism is an inherited disease, although some aspects of this complex disorder have been shown to be genetically determined. One might expect that genetic factors could influence either the tendency of an individual to drink excessively or the sensitivity of individuals to the effects of a given alcohol intake, or both. Most genetic work has dealt with drinking behaviour. For example, it is well known that inbred strains of mice differ in voluntary alcohol intake¹. In man, twin studies have shown higher concordance in monozygotic than dizygotic pairs with respect to patterns of drinking^{2,3}. Alcoholism is frequent among offspring of alcoholics, even when raised away from their biological parents^{4,5}. Genetic differences in sensitivity to acute effects of alcohol have been shown in mice⁶ and in human

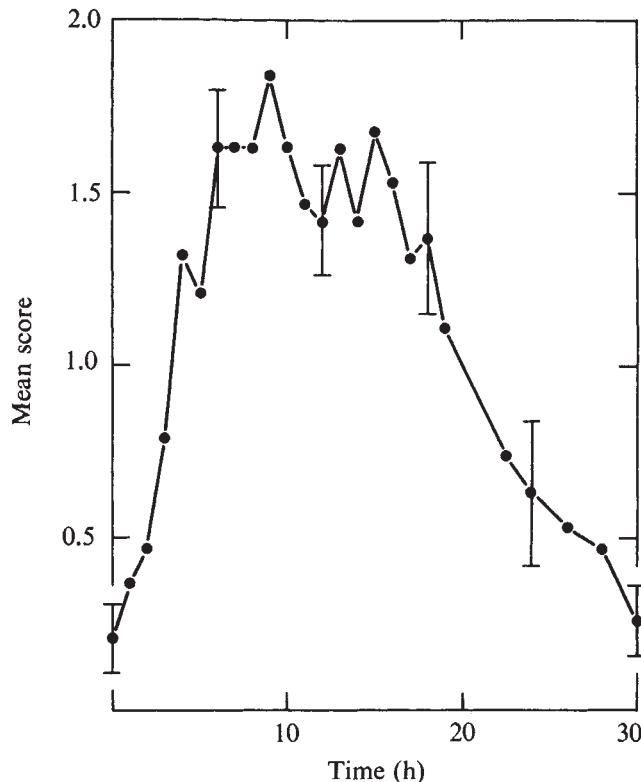


Fig. 1 Typical curve of withdrawal seizure scores against time after withdrawal. This curve is for the parental generation, males, second cycle. Points are mean scores for nineteen mice. Vertical bars indicate the s.e.m. at several points along the curve. The area under this curve is 32.1 units (score $\times$ h).

populations (Caucasoid compared with Mongoloid)⁷. I report here that genes influence the severity of alcohol withdrawal effects in mice. This may mean that vulnerability to physical dependence can be inherited.

Three generations of mice were tested for severity of withdrawal convulsions after a standard regimen of alcohol administration. From the parental generation we selected animals that showed consistently high or consistently low "withdrawal scores" and data obtained from two generations of their offspring showed that these differences could be inherited.

Male and female Swiss-Webster mice were subjected to two cycles of intoxication and withdrawal, using methods developed in this laboratory^{8,9}. The cycles were 6 weeks apart. In each cycle blood alcohol concentrations of about 1.8 mg ml⁻¹ were maintained for 3 d by inhalation of alcohol vapour (11 mg l⁻¹). Blood alcohol levels were monitored using an enzymatic assay method¹⁰. The mice were given daily injections of pyrazole (1 mmol kg⁻¹) intraperitoneally to inhibit alcohol oxidation and stabilize blood alcohol concentrations. On withdrawal, the mice were tested repeatedly for convulsions elicited by handling, and the seizures were scored by a

Table 1 Parental Generation

	Blood alcohol (mg ml ⁻¹)			Withdrawal score		
	Males (N=19)	Females (N=18)	Both sexes	Males	Females	Both sexes
Cycle 1	1.85 $\pm$ 0.066	1.59 $\pm$ 0.051	1.72 $\pm$ 0.047	38.6 $\pm$ 2.31	25.7 $\pm$ 3.06	32.3 $\pm$ 2.16
Cycle 2	1.94 $\pm$ 0.071	1.84 $\pm$ 0.075	1.89 $\pm$ 0.051 †	32.1 $\pm$ 3.36	29.3 $\pm$ 4.12	30.8 $\pm$ 2.62
Both cycles	1.90 $\pm$ 0.049	1.71 $\pm$ 0.049 *	1.81 $\pm$ 0.036	35.3 $\pm$ 2.08	27.5 $\pm$ 2.55 ‡	31.5 $\pm$ 1.69

Blood alcohol concentrations were estimated in from one to three assays per mouse per cycle. The data are means $\pm$ s.e.m.

* Male compared with female blood alcohol concentrations, $P < 0.01$, Student's t test.

† Cycle 1 compared with cycle 2 blood alcohol concentrations, $P < 0.05$.

‡ Male compared with female withdrawal scores, $P < 0.05$.

Table 2 Withdrawal Scores of Mice chosen for Breeding

Group	Mouse No.	Withdrawal score		Group mean $\pm$ s.e.m.
		Cycle 1	Cycle 2	
High	Male 1	61.8	76.4	55.0 ± 3.95
	Male 2	45.2	48.9	
	Female 1	50.5	64.0	
	Female 2	46.3	47.3	
Low	Male 3	30.0	14.1	$14.9 \pm 3.58^*$
	Male 4	22.7	23.0	
	Female 3	16.0	9.4	
	Female 4	2.0	2.0	

The data are scores of eight mice in both replications of the experiment shown in Table 1.

* High group compared with low group, $P < 0.001$, Student's t test.

standard rating system. We have previously published evidence that these convulsions represent physical dependence on ethanol, that they can be reliably scored by different observers, that they are not due to pyrazole, and that they do not occur in normal Swiss-Webster mice^{8,9,11,12}. Figure 1 shows a typical plot of scores against time. A numerical estimate of the intensity of the withdrawal reaction was obtained by computing the area under the curve, in units of score multiplied by hours. Areas were separately computed for individual mice, to allow statistical comparisons between groups. The area under the curve is referred to below as the "withdrawal score".

When mice of both sexes were exposed to alcohol in the same vapour chamber, the males developed higher blood alcohol concentrations than the females (Table 1). Clearly,

either the alcohol or the pyrazole was metabolized differently by the two sexes. During withdrawal, the males showed higher seizure scores than the females, as would be expected from the blood alcohol concentrations⁹. Withdrawal scores were the same in the two cycles. The most important observation was that some individual mice scored high in both cycles and others scored low. We therefore chose for breeding two pairs of high-scoring and two of low-scoring mice. Their withdrawal scores are shown in Table 2. The "highs" all had scores of more than forty-five units in each cycle and the "lows" scored thirty units or less. The groups differed significantly in withdrawal scores. Blood alcohol concentrations were 1.96 ± 0.086 (s.e.) and 1.78 ± 0.125 for the high and low group respectively, not a significant difference.

Offspring of the two pairs of high-scoring mice (five males and six females) were designated "H", and offspring of the two low-scoring pairs (three males and six females) were designated "L". These twenty mice were given the same alcohol exposure and withdrawal scoring as their parents. All mice lost some weight during the intoxication period, as in previous experiments with alcohol inhalation. The mean weight loss was 9% for males and 5% for females and there was no difference in weight loss between the H and L groups.

As Table 3 shows, the sex difference in blood alcohol levels was similar to that of the parents. Within each sex, the H group scored two to three times higher than the L group. Multiple regression analysis was used to assess separately the effects of score group (H compared with L), sex and blood alcohol levels on the withdrawal score (dependent variable). The results showed that withdrawal scores varied with blood alcohol levels as expected and also differed significantly between the H and L groups. There was no sex difference in

Table 3 F₁ Generation

	Blood alcohol (mg ml ⁻¹)			Withdrawal score		
	Males	Females	Both sexes	Males	Females	Both sexes
High	2.60 ± 0.119 (5)	1.72 ± 0.096 (6)	2.12 ± 0.156	40.8 ± 6.64	23.1 ± 4.09	31.1 ± 4.50
Low	2.37 ± 0.201 (3)	1.59 ± 0.063 (6)	1.85 ± 0.149	20.6 ± 8.33	7.5 ± 2.15	11.9 ± 3.54
Both groups	2.52 ± 0.106	1.65 ± 0.058	2.00 ± 0.110	33.2 ± 6.06	15.3 ± 3.22	22.5 ± 3.62
Multiple regression analysis of withdrawal scores						
Independent variable	Regression coefficient $\pm$ s.d.		t	P		
Group	6.15 ± 2.03		3.03	<0.01		
Sex	4.79 ± 4.11		1.1	NS		
Blood alcohol	30.10 ± 8.65		3.48	<0.01		

Blood alcohol concentrations were computed from daily assays for each mouse. Data in the upper half of the table are means $\pm$ s.e.m. for the number of mice shown in parentheses. NS, not significant.

Table 4 F₂ Generation

	Blood alcohol (mg ml ⁻¹)			Withdrawal score		
	Males	Females	Both sexes	Males	Females	Both sexes
High	2.15 ± 0.114 (10)	1.64 ± 0.089 (5)	1.98 ± 0.102	51.8 ± 3.82	41.9 ± 3.66	48.5 ± 3.01
Low	2.05 ± 0.093 (5)	1.74 ± 0.173 (12)	1.83 ± 0.128	19.0 ± 5.51	11.7 ± 3.91	13.9 ± 3.22
Both groups	2.12 ± 0.081	1.71 ± 0.123	1.90 ± 0.083	40.9 ± 5.12	20.6 ± 4.50	30.1 ± 3.80
Multiple regression analysis of withdrawal scores						
Independent variable	Regression coefficient $\pm$ s.d.		t	P		
Group	15.76 ± 2.11		7.47	<0.001		
Sex	1.85 ± 2.32		0.80	NS		
Blood alcohol	11.97 ± 4.71		2.54	<0.05		

Blood alcohol concentrations were computed as in Table 2. The data are means $\pm$ s.e.m. for the number of mice shown in parentheses. NS, not significant.

withdrawal scores when blood alcohol levels were taken into account. Thus a significant difference in intensity of withdrawal reactions, corresponding to the parents, was evident even in the first generation.

Two pairs of highest-scoring F1 mice from the H group and two pairs of lowest-scoring F1 mice from the L group were bred. The progeny (fifteen males and seventeen females) were exposed to alcohol vapour for 3 d and scored in withdrawal as before. Again, the weight loss during intoxication was the same for the H and L groups. In this experiment we attempted to obtain the same blood alcohol levels in both sexes to compare their withdrawal scores directly. Therefore, the females were exposed to slightly larger concentrations of alcohol vapour than the males (12.5 mg l⁻¹ for females, 10.9 for males). This, however, proved insufficient to abolish the sex difference in blood alcohol concentrations (Table 4). As before, the multiple regression computation, taking the different blood alcohol levels into account, showed no sex difference in withdrawal scores. By contrast, the H and L groups differed markedly ($P < 0.001$) in withdrawal reaction intensity.

These experiments demonstrate that susceptibility to seizures on withdrawal of alcohol can be inherited. Further work will be necessary to show whether the effect is specific for alcohol. At least three possibilities should be examined: (1) mice differ in their ability to develop physical dependence, that is, to produce a biochemical change in the brain in response to ethanol; (2) mice differ in the intensity of seizures evoked by a given change in brain biochemistry; and (3) mice differ in baseline excitability of the central nervous system before exposure to ethanol. Inbred strains of mice are known to differ in susceptibility to various types of seizures¹³, an observation that may pertain to the second or third possibility. Any of these mechanisms might help to explain why individuals respond differently to chronic administration of alcohol.

These data also suggest that there is no sex difference in susceptibility to alcohol physical dependence in mice. Sex differences in withdrawal scores were entirely accounted for by differences in blood alcohol levels. This observation is interesting in connexion with the well-known higher incidence of alcoholism in men than in women, a phenomenon that might be either genetic or cultural.

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Erythrocytes from Animals with Genetic Muscular Dystrophy

EFFECTS of congenital muscular dystrophy include changes in processes associated with membrane systems of muscle^{1,2}. Moreover, there is evidence that genetic dystrophy in mice, which appears to be a suitable model for the human disease³, is associated with alteration of membrane events occurring in other tissue as well⁴⁻⁸. For example, we have reported altered proton permeability and related functions in liver mitochondria isolated from animals with the disease⁵. As aberrant membrane permeability could lead to the pathological state of muscle by producing defective excitation coupling, it is interesting to examine other tissues for evidence of systemic membrane dysfunction. We report here surface alterations of erythrocytes from dystrophic mice as revealed by scanning electron microscopy.

Mice of strains 129/ReJ (normal), 129/ReJ-dy (dystrophic) and C57Bl/6J-dy^{2J} (dystrophic) from the Jackson Laboratories, Bar Harbor, Maine, were killed by decapitation, and arterial blood was removed with a micropipette. The blood was diluted ten-fold in isotonic saline containing 0.5% glutaraldehyde. After incubation for 1 h at 25°, the cells were sedimented at 1,000g for 10 min, washed three times with isotonic saline, and finally diluted to 2.0 ml. A small volume of cell suspension was placed on a 'Millipore' filter of 0.22 μ m pore diameter and washed with a drop of isotonic saline. Pieces of filter were fixed to copper stubs with silver conductive paint, coated with approximately 200 Å of gold-palladium (40-60%) and examined with a Jeolco JSM-2 scanning electron microscope at 20 kV.

Figure 1 shows a field of cells obtained from a normal animal (A) and from a dystrophic littermate (B). It is evident that a large proportion of the cells in the dystrophic case show surface irregularities involving variable protrusions from the cell surface, while cells from the normal animal do not. Table 1 summarizes electron microscopic examination of twenty animals and shows a high incidence of distorted cells in dystrophic mice of two different strains. Distortion of the cell surface was also observed when the cells were incubated, washed, and suspended in either hypotonic or hypertonic saline solution. Finally, in each of the ten littermate pairs of mice examined, there was a correlation between erythrocyte surface distortion and dystrophy.

It seems to be significant that the defect in cell surface was observed in mice of two genetically distinct dystrophic strains⁹. In this connexion, it is worth noting that we have also recently found similar alteration in erythrocytes from rats rendered dystrophic by maintenance on a diet deficient in vitamin E.

The observation of considerable alteration in the surface of erythrocytes from dystrophic mice, together with the discovery of altered liver mitochondrial permeability⁵, suggests that serious consideration should be given to the hypothesis linking genetic dystrophy and systemic alteration of cellular membranes. A systemic defect in membrane composition could, for example, produce a corresponding defect in cation permeability which would be expected to have graver consequences in muscle, where excitation-coupling depends on cation fluxes, than in many other tissues. If a membrane defect that underlies dystrophy is

Table 1 Percentage of Distorted Erythrocytes in Normal and Dystrophic Mice

Strain	No. of animals	No. of cells counted	% distorted
129/ReJ (normal)	10	294	4.1
129/ReJ-dy (dystrophic)	8	187	51.6
C57Bl/6J-dy ^{2J} (dystrophic)	2	78	26.9

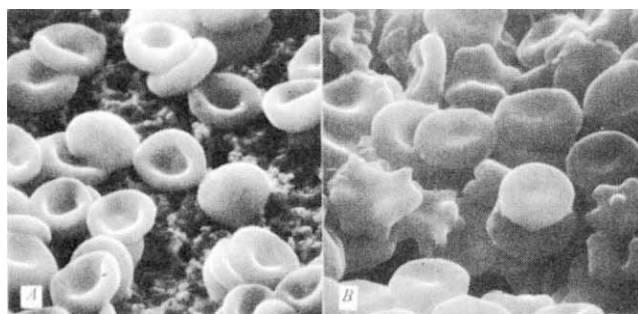


Fig. 1 Scanning electron micrographs of erythrocytes. A, Normal mouse; B, dystrophic mouse, strain 129/ReJ-dy. In both instances magnification is 2,500-fold.

indeed widely distributed in the tissues of the organism, then it is likely that it should be sought in tissues other than muscle, as the characteristic degeneration of muscle renders judgments about membrane function virtually impossible.

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Odour-Blindness to Musk: Simple Recessive Inheritance

Whissell-Buechy and Amoores¹ have reported specific anosmia in humans to two substances, iso-valeric acid and a musk (pentadecalactone), anosmia to the second being inherited as a recessive. They found a difference of incidence in both anosmias between Black and Caucasian subjects.

This work raises several points of biological interest as both iso-valeric acid and musks are candidates for consideration as functional pheromones, the former in monkeys^{2,3}, and both of them in man⁴. It is also believed that some components of olfactory response to musk odours (exaltolide^{5,6} and Δ^{16} -androstene or "boar odour") are hormone-dependent, being markedly increased by oestrogens. Exaltolide perception in women has been said to vary with the menstrual cycle⁶.

Whissell-Buechy and Amoores's sample consisted, for pentadecalactone, of 218 parents and 266 children ranging in age from 5 to 18 yr. These results were not broken down by sex and puberty, but of fifteen anosmic parents cited in their figure, ten were women and five were men, assuming the convention that circle symbols represent females. The object of Amoores's

study is to use genetic and chemical mapping to investigate primary odour response. On the crude data, and accepting the idea of menstrual variation, it could be that the genetic effect identified in the case of pentadecalactone is an unusually high degree of oestrogen dependence rather than a primary anosmia.

I suggest that in future studies involving potential pheromones it would be interesting to follow anosmic female subjects throughout a complete menstrual cycle and anosmic children through puberty. Anosmia for iso-valeric acid would not be expected to have in man the effects on sexual performance which it might have in monkeys², but any anosmia, whether total or cyclical, affecting potential pheromones is of special interest. It would also be desirable to look for evidence of androgen effects upon the ability to detect, or upon the nature of the subjective response to, vaginal fatty acids, and to re-examine Whissell-Buechy and Amoores's data by age, sex, and the ingestion of hormones, particularly oral contraceptives, as well as by menstrual date. It is known that the perception of taste and odour stimuli can be profoundly affected by, for example, pregnancy, at the level of subjective response rather than of threshold.

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Drs Whissell-Buechy and Amoores reply: We are glad that Dr Comfort¹ has pointed out some wider biological significance of the variations in odour sensitivity that we have described². Many of his suggestions for future study are included in new research that we have just begun. At present we merely wish to counter his argument that our observed distribution of pentadecalactone anosmia in families could possibly have been due to a menstrual variation in sensitivity of females, rather than having a recessive genetic basis as we believe.

It should be borne in mind that about half our subjects were male, and that a good proportion of the females were either prepubertal or postmenopausal. Therefore, it is difficult to see how any reported menstrual cyclic changes in musk sensitivity³ could account for our results, except in those few of our families where the incidence of anosmia was limited to nubile females. Although eleven mothers and only six fathers were musk anosmics, the difference is not significant. We should also mention that the eighty-four unrelated adult non-anosmic subjects in Fig. 1 of our paper² included fifty-two men and thirty-two women, but the mean thresholds of the two groups to pentadecalactone were not significantly different. This confirms an earlier report by one of us⁴. It means that our family trees cannot even be ascribed to any supposed systematic difference between the sexes as regards sensitivity to musk.

We raise this point because it conflicts with Le Magnen's⁵ widely-quoted assertion that men, boys, and prepubertal girls are much less sensitive than adult women to the odour of pentadecalactone musk. We find that young boys and girls (5–11 yr) also can undoubtedly smell this compound, unless they happen to be among the 8–10% having this specific anosmia, which is equally likely to affect their seniors. We are in the course of gathering additional quantitative data on this interesting topic. Meanwhile we continue to believe that a

recessive genetic trait remains the best available explanation for our results.

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Evidence for the Theory of Dual Hypothalamic Control of Ovulation

THE hypothalamus is rich in monoamines including serotonin (5-HT) and catecholamines (dopamine, adrenaline and noradrenaline). It has been reported that an injection of 5-HT into the third ventricle inhibits the secretion of gonadotrophins in cyclic and bilaterally ovariectomized rats¹⁻³ and elevated levels of 5-HT in the hypothalamus interfere with both gonadotrophically induced^{4,5} and spontaneous ovulation^{6,7}. On the other hand, intraventricular injection of dopamine¹ or its metabolite adrenaline⁸ promotes gonadotrophin secretion and/or ovulation. On the basis of these and other results it has been postulated that the hypothalamus exerts a dual control over ovulation—its inhibitory influence being transmitted via a 5-HT pathway and a stimulatory one through a catecholaminergic (CA) pathway. It is believed that the balance between these contrasting influences determines the occurrence of ovulation—a certain critical balance in favour of the CA pathway promoting ovulation, and the opposite inhibiting it⁶⁻¹¹. How these contrasting influences interact to regulate ovulation during the reproductive cycle is not known. We therefore injected monoamines or their antagonists into the third ventricle of immature rats primed with gonadotrophin and given a single injection of progesterone, and studied the effects of these procedures on ovulation. It is well documented that the facilitatory effect of progesterone on ovulation in such rats is exerted at the hypothalamic level, because barbiturates^{12,13} or hypothalamic lesions¹⁴ can block ovulation induced by progesterone.

Immature rats (65–70 g, 28-day-old) of the Sprague-Dawley strain were maintained under controlled conditions of light (on from 06.00–18.00 h) and temperature (71° F) and provided free access to food and water. Rats received a single subcutaneous injection of 5 IU of pregnant mare's serum gonadotrophin (PMSG, Equinex, Ayerst) in 0.1 ml saline at 11.00 h on day 29 followed by a single subcutaneous injection of 1.0 mg of progesterone (0.2 ml oil, Sigma Co.) 24 h later. Under our conditions the "critical period", that is, the period during which the neurogenic activation of the anterior pituitary occurs, extends from 14.00 h to 16.00 h on the day of progesterone injection as determined by pentobarbital sodium-induced inhibition of ovulation (unpublished data). On the following morning the animals were killed and both Fallopian tubes searched for ova. Rats were anaesthetized with ether on the morning or afternoon of the day of progesterone injection and placed in a stereotaxic instrument. Monoamines or their antagonists were injected into the third ventricle via a 27 gauge needle in a volume of 10 μ l of vehicle composed of propylene glycol-saline (1:1, v/v). The sham operated animals received vehicle alone. When two different agents were administered they were given together in the same volume (10 μ l). The position of the cannula was verified at autopsy in the initial experiment using thirty-five rats. Of these, only two of the cannulae were misplaced. In subsequent experiments, therefore, the position of the cannula was not verified.

Injection of PMSG alone failed to induce ovulation (group A, Table 1) but an additional injection of progesterone 24 h later induced a full ovulatory response in 100% of the animals (group B), thus confirming the well established facilitatory effect of progesterone on ovulation in these animals¹². Intraventricular injection of vehicle alone 1–2 h after progesterone injection, that is, approximately 1 h before the onset of the "critical period" under our conditions, did not interfere with progesterone induced ovulation (group C) whereas an injection of an α -adrenergic blocker, phenoxybenzamine (group D), blocked the facilitatory effect of progesterone. When a β -adrenergic blocker, propranolol, was substituted it failed to inhibit ovulation (group E). These results demonstrate that the facilitatory effect of progesterone on ovulation is transmitted through an α -adrenergic pathway. Thus following progesterone injection the balance between 5-HT and CA systems must be in favour of the latter. If the balance between these contrasting influences is crucial in ovulation, then maintaining the balance in favour of the 5-HT system ought to interfere with the facilitatory effect of progesterone. This indeed proved to be the case as 100 μ g of 5-HT creatinine sulphate (equivalent to 45 μ g

Table 1 Effects of Intraventricular Injection of Monoamines and their Antagonists on Progesterone Induced Ovulation in Immature Rats primed with PMSG (Mean $\pm$ s.e.)

Group and treatment	Body weight at autopsy (g)	No. of rats ovulating	Inhibition of ovulation (%)	Ova
		No. treated		Ovulating animal
(A) PMSG, 5 IU	76 ± 1	0/10	100	0
(B) Control	80 ± 1	11/11	0	10.0 ± 0.8
(C) Sham control, 10 µl *	74 ± 2	5/5	0	11.1 ± 1.4
(D) Phenoxybenzamine, 100 µg †	76 ± 1	1/5	80	13
(E) Propranolol, 100 µg †	79 ± 2	5/5	0	8.6 ± 1.8
(F) 5-HT, 100 µg	71 ± 1	2/10	80	8.0 ± 2.0
(G) 5-HT + LSD, 2 µg	78 ± 2	10/10	0	10.1 ± 0.9
(H) 5-HT + dopamine, 100 µg	72 ± 2	9/10	10	10.3 ± 0.7
(I) Starvation ‡	61 ± 1	6/6	0	9.2 ± 0.8

All rats received 5 IU PMSG on day 29. In addition, groups B to I received 1 mg progesterone 24 h later, that is, at 11.00 h. Within 2 h after the steroid injection monoamines or their antagonists were microinjected into the third ventricle under ether anaesthesia. Tubal ova were counted at autopsy 48 h after PMSG injection.

* Vehicle alone.

† Given 1 h before progesterone, that is, at 10.00 h.

‡ Food was withdrawn following PMSG injection until autopsy but water was available.

of 5-HT) injected 1 h before the critical period blocked progesterone induced ovulation (group E). Conversely, by shifting the balance of monoamines in favour of CA, ovulation ought to be restored even in the presence of high levels of 5-HT. The inhibitory effect of 5-HT was completely blocked by a simultaneous injection of LSD (group G), a potent antagonist of 5-HT¹⁵, or by dopamine (group H). These data should not necessarily be interpreted to mean that dopamine as such overcomes the inhibitory effect of 5-HT. It is equally possible that its metabolites adrenaline or noradrenaline may be involved. The possibility that the intraventricularly administered monoamines act on the pituitary can be excluded because monoamines do not inhibit the response of the pituitary to gonadotrophin releasing factors *in vitro*¹⁶, nor do they significantly affect discharge of gonadotrophins from the pituitary when infused directly into the portal vessels in the pituitary stalk³. Body weight was unaffected by these treatments, so the nonspecific stress of the drugs cannot account for the observed effects. In fact, starving the animals beginning at the time of PMSG injection until autopsy, which caused a considerable loss of weight, failed to interfere with the facilitatory effect of progesterone on ovulation (group I).

Our results provide evidence for the first time that the inhibitory effect of 5-HT on ovulation can be overcome by a catecholamine and suggest that the balance between these contrasting influences is crucial in ovulation. These findings further reinforce the theory of dual hypothalamic control of ovulation postulated earlier⁶.

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Lateral Interaction between Neural Channels sensitive to Texture Density?

A NUMBER of well-known visual phenomena, including Mach Bands¹ and the related illusion² shown in Fig. 1 are interpretable as evidence of lateral interaction between adjacent neural channels sensitive to retinal luminance. Inhibitory interaction would lead to disproportionate weight being given to sharp discontinuities in luminance. This can be taken to explain why the middle panel in Fig. 1 (when viewed from the right distance) is seen as brighter overall than its neighbours, though objectively all three have the same luminance at their centres. The limited retinal range of the interactive process

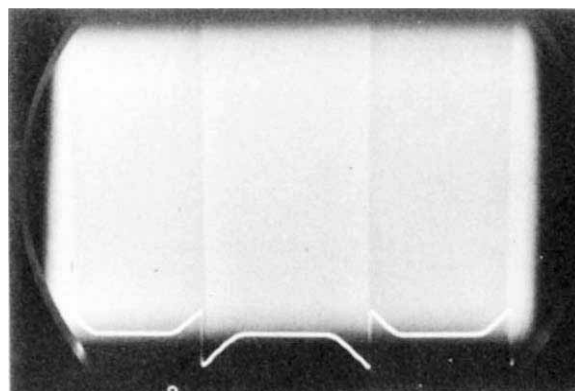


Fig. 1 Lateral interaction between channels sensitive to luminance. This figure illustrates the well-known enhancement of brightness produced when a given luminous area is flanked by regions whose luminance profile is as shown at the foot. (Downward deflexion represents increased luminance.) The role of the transition regions in generating the illusion is strikingly demonstrated by covering them with strips of plain paper.

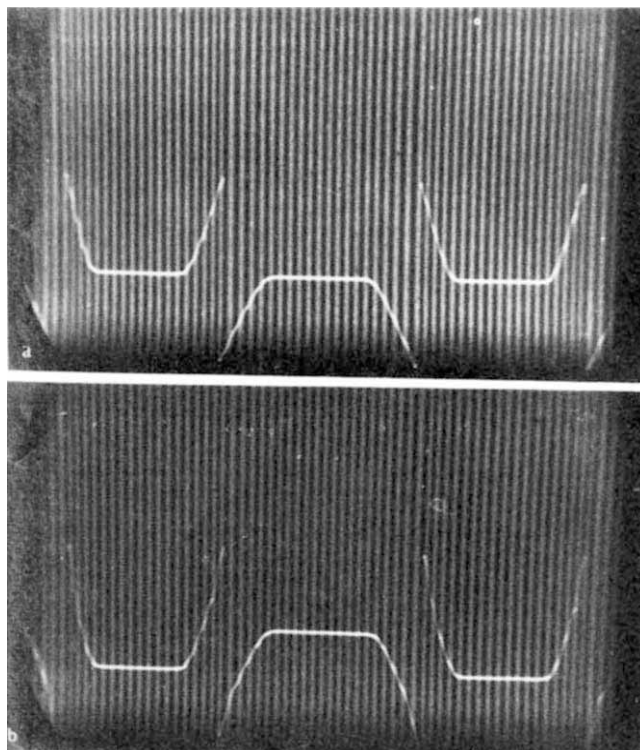


Fig. 2 Lateral interaction between channels sensitive to texture density. (a) The texture density (spatial frequency) of each pattern of lines is modulated in the same way as luminance was in Fig. 1. The height of the superimposed oscilloscope trace is linearly related to spatial frequency (upward deflexion for increased frequency). Closely analogous contrast enhancement effects can be observed. (b) By adding a central "pedestal" to the controlling waveform, the effect can be annulled and so quantified.

responsible is shown by the gradual disappearance of the illusion as the viewing distance is increased.

Gibson³ and others have shown psychophysically that the gradient of density of visual texture is an important clue to the orientation in depth of textured surfaces. This suggests that the visual nervous system might also have a gradient-enhancing process acting among elements sensitive to density of texture⁴. If so, one might expect analogous border contrast effects to those of Fig. 1 in the spatial-frequency domain giving rise to illusory spatial frequency shifts near discontinuities of texture density. In the experiments to be described these expectations were confirmed.

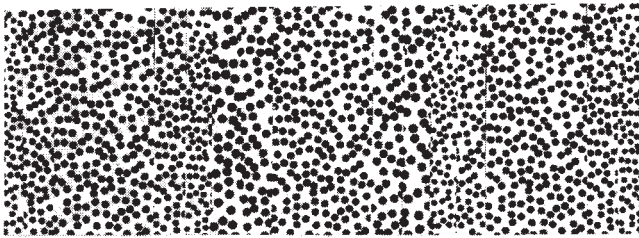


Fig. 3 A static visual noise field with similar variations in texture density to those in Fig. 2a.

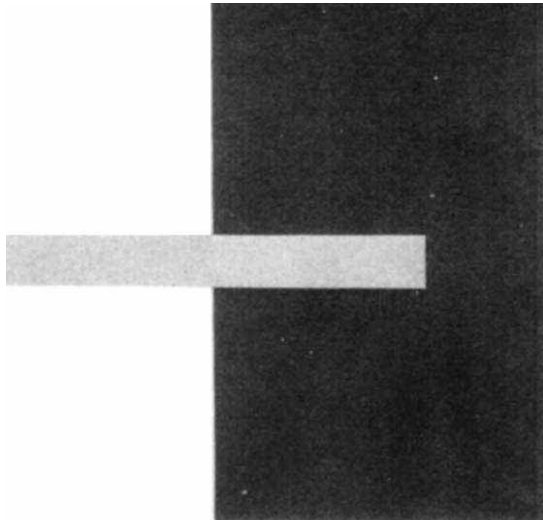


Fig. 4 Simultaneous contrast of brightness. A thin black line bisecting the test strip enhances the effect. If the line is moved transversely to and fro it seems to draw the light/dark boundary with it.

For ease of adjustment the first stimulus used consisted of a frequency modulated grating (Fig. 2a) on the screen of a cathode ray tube. X-Deflexion was provided by a normal time-base generator at 50 Hz. A 100 kHz triangular waveform provided Y-deflexion. Trace brightness was modulated by a periodic trapezoidal waveform whose frequency was varied electronically with X-coordinate according to the profile shown at the foot of Fig. 2a. This arrangement avoided any change in mean luminance with spatial frequency, which might otherwise have produced confusing side effects.

The resulting pattern in Fig. 2a produces the expected illusion of spatial frequency shift, the central panel appearing 5–10% lower in spatial frequency than its neighbours. To quantify this effect, the difference between resting levels of the modulating waveform was made adjustable by a smooth knob, which the subject was asked to turn until the line densities at the centres of all three panels looked the same. A typical stimulus approximately adjusted for perceived equality is shown in Fig. 2b, with its actual density profile at the foot for comparison. As with Fig. 1, the strength of the illusion can be seen to depend on the visual angle subtended by the transition regions. With the profiles shown, a subtense of about 0.5° per region seems optimal. Interestingly, the effect is less when the figure is turned through a right angle.

To test the generality of this effect, a random dot field with roughly similar gradations of texture density was constructed from a series of strips printed at different magnifications (Fig. 3). This gives only a crude stepwise approximation to the texture density profile of Fig. 2a; but for most observers it produces a weak illusion in the same direction. The middle

panel seems coarser in texture than its neighbours, though in fact the central regions of all are identical. In most cases the strongest effect was observed when the transition region subtended about 1° at the eye.

The phenomenon of "simultaneous contrast" illustrated in Fig. 4 has long been taken as evidence of lateral inhibition between luminance-sensitive channels. Left and right halves of the central test strip, identical in luminance, look different in brightness. Analogous test patterns were therefore prepared in which contrasting densities of texture were juxtaposed. Inspection of Fig. 5 shows that (a) enhancement of texture

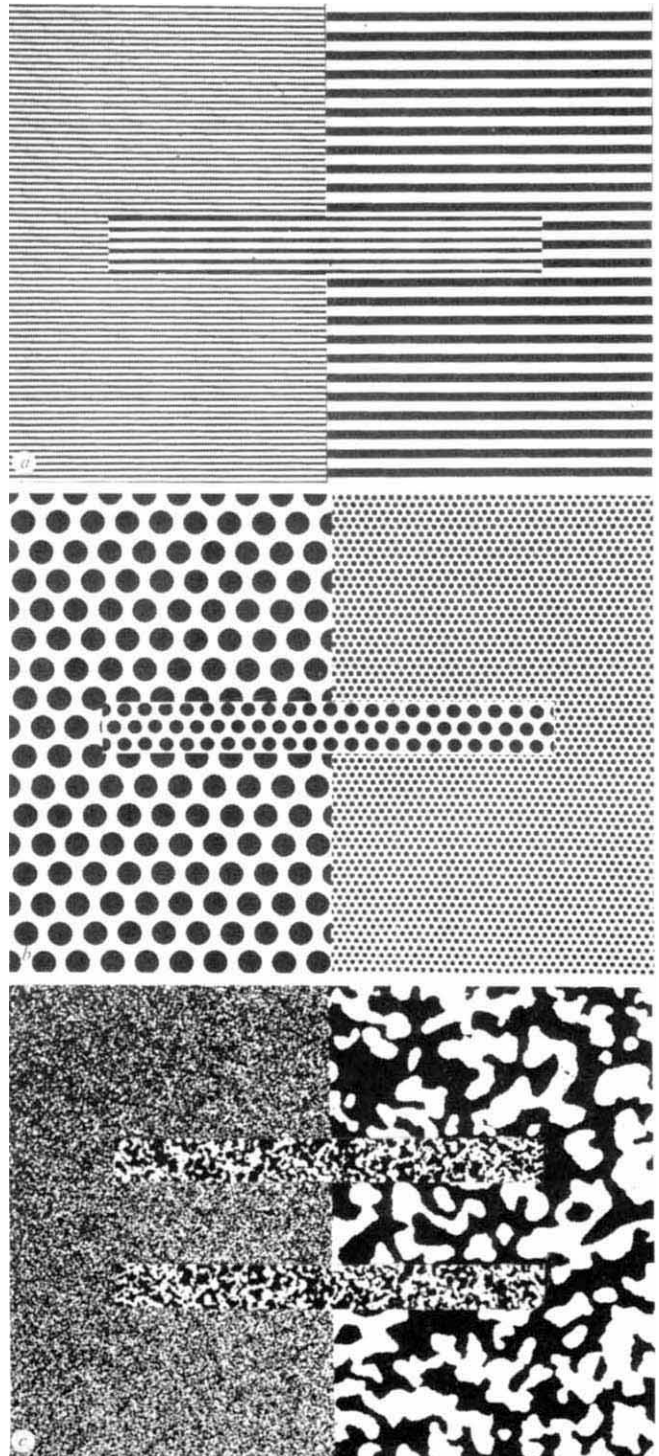


Fig. 5 Simultaneous contrast of density of texture. Moving a dividing line over the test strip has analogous effects in each case. Note that (c) has two identical half strips lying in opposite directions for comparison.

contrast does occur, and obeys laws closely analogous to those of brightness contrast; and (b) such phenomena are not peculiar to stimuli with well-defined spatially periodic and oriented components. In both cases, the contrast seen is enhanced if a thin black dividing line (such as a piece of wire) is placed along the vertical mid-line of the figure. If the line is moved to and fro it "draws" the area of magnified or minified texture density with it.

The contrast can be further enhanced by moving the whole figure up and down while the eye is held stationary. This suggests that the neural channels involved (like many feature-sensitive units already identified physiologically) are more responsive to moving than to stationary retinal images.

If the central "test strip" of one of these figures is presented to one eye and the remainder to the other, it is possible with practice to combine the images dichoptically. No significant contrast effect is then observed. This suggests that the abstraction of texture density takes place at a relatively early stage in the neural processing of retinal signals, and that the lateral inhibitory mechanisms presumably responsible for these contrast enhancements are located mainly in the unocular systems before binocular fusion.

In summary, it seems from these experiments that the visual system may have channels that signal local density of texture, and interact to enhance local gradients of texture density, in ways somewhat analogous to the channels that are sensitive to retinal illumination and its gradients. Such "texture" channels would not require to be "space-frequency tuned" like those postulated by Campbell and Robson⁵. They might, however, play a part in the "binocular perception of depth without geometrical cues" described recently by Fiorentini and Maffei⁶, who found that changes in contrast in one eye could produce similar effects to changes in spatial periodicity. This, like the effects described here, would be readily understandable if the channels concerned respond monotonically to density of texture elements over a certain range. Some geniculate cells recently discovered⁷ seem to have properties of this general kind.

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Transcellular Strands of Cytoplasm in Sieve Tubes of Squash

THE mechanism of long-distance phloem translocation is the subject of several hypotheses based on different concepts of structure and function in sieve tubes¹. One of us (R. T.)²⁻⁴ has proposed that transcellular strands of cytoplasm, continuous from one sieve element to the next through the sieve pores, provide a basis for the development of the physical force required for movement and pathways for translocation. The hypothetical model of a transcellular strand⁵ consists of closely packed filaments of phloem filament (PF)-protein which form a tubular boundary enclosing cytoplasmic particles and a substructure of one or more tubules parallel with the outer boundary and formed from endoplasmic membranes. The



Fig. 1 A longitudinal section (18 μ m thick) of a sieve tube viewed in the Nomarski microscope and showing parallel strands of cytoplasm, one of which (---) is easily followed through the sieve pore. The bar represents 10 μ m.

number of tubules in each strand depends on the diameter of the sieve pores filled by a single strand. Should a conformational change⁶ occur in the outer boundary and cause a constriction which travelled as a wave in response to the propagation of electrical impulses of regular periodicity, this peristaltic pumping action could impel solution through the enclosed sub-tubules.

Aikman and Anderson's theoretical analysis⁷ shows that the capacity and energy requirements of the strand system are consistent with measurements obtained from physiological experiments, but recent reviews^{1,8-10} question the evidence of transcellular strands in sieve elements and a number of research workers¹¹⁻¹⁷ are convinced these structures do not exist. Their main criticisms are that evidence in favour of transcellular strands is sparse and is largely from light micrographs of fresh hand sections and that electron microscopy of the sieve elements has failed to provide evidence of highly organized transcellular strands. Lee *et al.*¹⁸ did not see transcellular strands when they used the differential diffraction microscope (Nomarski) to observe sieve tubes of *Heracleum mantegazzianum* which were in narrow bands displaced from surrounding tissues with both ends attached to a petiole. In a study of freeze-etched sieve tubes Johnson¹⁹ reports transcellular strands. He presents evidence of parallel groups of filaments at sieve pores and in the lumina of sieve elements, but contrary to the model described above he found no membranes.

Here observations of transcellular strands, obtained from cryostat sections in transmitted light^{20,21}, are extended using the



Fig. 2 *a*, An electron micrograph from a transverse section of a sieve plate in which pores have a tubular lining of densely stained material. The bar represents 2 μ m. *b*, An electron micrograph from a longitudinal section showing a strand extending from a sieve pore (SP) into the sieve element. W, Sieve tube wall. Black arrow, plasmalemma; White arrow, a group of parallel structures which can be followed from the constricted end of the broken strand (see text). The bar represents 2 μ m.

Nomarski microscope (Fig. 1). For the electron microscopy, a new method of fixation and dehydration was developed. A panel was cut in a stem internode of *Cucurbita pepo* cultivar Golden Hubbard, and the inner phloem and xylem of one vascular bundle were stripped away so that the outer phloem (about 1.0×1.5 mm in cross section, 40 mm long) could be separated from most surrounding cortex without moving the strip from the position it occupied in the plant. The free phloem and surrounding stem tissue, still attached to the otherwise intact plant, were then plunged into 'Freon 12' pre-cooled with liquid N₂, and frozen pieces of phloem were placed in a freeze drier at -100° C. The temperature of the tissue rose to -70° C after 135 min and to -60° C during the next 120 min. Air was admitted to the drying chamber and the specimens were transferred into 2% OsO₄ at 5° C, dehydrated in 90% and 100% ethanol and embedded by standard epoxy procedure (Fig. 2).

Figure 1 is a cryostat section showing a sieve plate and a sectional view of one sieve pore. Below the plate seven strands seem to be displaced toward the sieve tube wall. Above, at least ten strands are orientated with the long axis of the sieve tube and, near the sieve plate, are uniformly distributed across the cell lumen. With one exception, the strands are much narrower than the width of the pore. This we interpret as being due to their collapse and loss of contents during preparation. The exceptional strand does not reveal any contents but at its widest is the same width as the pore. Both boundaries of this strand can be easily followed through the sieve pore.

Figure 2*a* is an electron micrograph of a transverse section through three sieve pores. Three distinct layers may be seen to follow the contours of the pores. The first is an integral part of the sieve plate, the second is a narrow band of callose and the third is a heavily stained ring of material surrounding a comparatively empty space.

Figure 2*b* is an electron micrograph of a longitudinal section showing a strand with a discrete boundary and cytoplasmic contents on one side of a plate extending from a sieve pore into the lumen of the sieve tube. The three layers at the sieve pore can again be recognized. The heavily stained ring of Fig. 2*a* corresponds to the heavily stained constriction at the broken end of the strand within the pore. In the strand extension into the lumen two spherical organelles similar to small (0.6 μ m) mitochondria occur, and nearby a group of parallel structures (white arrow) can be followed from the constricted end of the broken strand and seems embedded in a mass of fine granules. Across the broken end there are more than ten indistinct holes with similar elliptical profiles (diameter about 90 nm). The linear structures in the lower half of the strand give an impression of straight-sided sub-tubules and may be partially degraded endoplasmic membranes.

On the right side of the strand the boundary separating the contents from the surrounding fibrillar material consists of a lightly stained band about 100 nm wide between two uniformly spaced lines with diameters of 25 nm which are much

wider than the plasmalemma (black arrow) but are similar in their staining properties. This highly organized boundary is best preserved near the sieve pore and is quite distinct from the plasmalemma which, in the absence of callose, lies against the surface of the sieve plate and the walls of the pores. Away from the pores, the dark double line, and the material between, spreads out into a much wider band of parallel filaments.

In agreement with the report of Jarvis *et al.*²¹, strands in Fig. 1 occur on both sides of the sieve plate and one of them is easily followed through a pore. This eliminates the possibility that strands might be formed by extrusion through sieve pores, for one would then expect a build-up of material on one side of the plate and strands on the other. The displacement of strands in Fig. 1 toward the sieve tube wall was possibly due to a lateral flow when phloem pressure was released by freezing. A lateral flow could not contribute to formation of the longitudinally orientated structures which we interpret as the damaged remains of strands that existed *in vivo*. In some preparations strands similar to those shown in Fig. 1 occurred in 80% of sieve elements. Cryostat sections gave the same results when mounted in a biochemical buffer containing a protein-reducing agent²² or in buffered glutaraldehyde. There seems little reason therefore to suppose that strands are produced by reactions between sieve tube contents and chemical fixatives during thawing of the frozen sections.

It can be argued that strands are an artefact produced during dissection or freezing²³. This possibility was considered in relation to different speeds of freezing²¹ but our results cannot be explained in this way because in cross section our strands repeatedly have a tubular profile which lines the sieve pores (Fig. 2*a* and unpublished results) and aggregations of PF-protein due to dissection or freezing would be undifferentiated and closely packed even if all lateral branching resulting from ice crystal formation were avoided. Further evidence of strands with straight-sided filamentous boundaries surrounding empty spaces of about the same diameter as the open space within a pore will be published later.

Figure 2*b* presents electron microscopic evidence of cytoplasmic constituents within a strand which we find convincing. Although this fragment of a strand was preserved at a pore, it seems that in less than 1 s during freezing, strands on the other side of the sieve plate were destroyed. This demonstration of the highly fragile nature of the strands explains why they are not found following the standard methods of chemical fixation in electron microscopy.

The hypothetical model⁸ is supported by evidence that parallel elements within the strand (Fig. 2*b*) seem to be derived from tubules formed from endoplasmic membrane. This result is consistent with Behnke's²⁴ discovery of endoplasmic tubular elements in sieve pores. The proposal that periodic constrictions in the outer boundary of a strand could induce a flow through the inner tubules becomes more credible with the evidence that the strand boundary seems to consist of protein filaments sandwiched between two membrane-like structures. The propagation of action potentials along membranes depends on the rapid depolarization of electrochemical potentials²⁵, which in sieve tubes could arise across membranes at the strand boundaries.

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An Anti-Inflammatory Peptide from Bee Venom

THE belief that the venom of the common honey bee, *Apis mellifera*, is beneficial in certain arthritic and rheumatoid conditions goes back to antiquity¹. In a study of phospholipase-A₂^{2,3} we have fractionated nearly 1 kg of freeze-dried bee venom and tested all the fractions for anti-inflammatory activity. Preliminary experiments showed activity to be associated with the basic peptide fraction. The peptides were separated using 'Sephadex' G25 and G50 followed by ion-exchange chromatography using either CM 'Sephadex' C25 (pH 4.7) or SE 'Sephadex' C25 (pH 4.2).

Activity was assessed using the rat paw oedema test^{4,5} and was found to be associated only with a peptide we called peptide 401. The dose response curve obtained is shown in Fig. 1 together with that obtained for hydrocortisone. It can be seen that peptide 401 is, in this test, about a hundred times more active than hydrocortisone.

Sequence determination showed that peptide 401 is identical to a peptide isolated by Breithaupt and Habermann⁶ and found

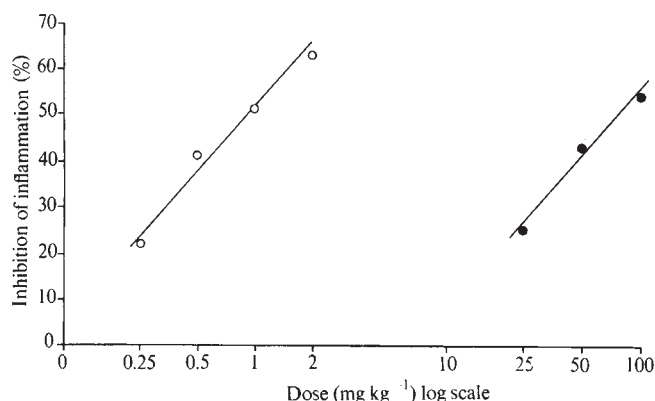


Fig. 1 Influence of peptide 401 (○) and hydrocortisone (●) on carrageenin induced oedema of the rat hind paw. Peptide 401 or hydrocortisone ('Solucortef', Upjohn), dissolved in physiological saline, was injected subcutaneously (1 ml per rat) into groups of five rats (♂ Wistar; Guy's Hospital strain) at the time of injection into the right hind paw of 0.1 ml of saline containing 1 mg of carrageenin (Marne Colloids Inc.). The increase in volume of the paw 5 h after injection of carrageenin when compared with the uninjected paw volume is a measure of inflammation. Comparison of the swelling in control groups given saline with those treated with peptide 401 or hydrocortisone gives a measure of anti-inflammatory activity, expressed here as % inhibition of inflammation (paw volume increase).

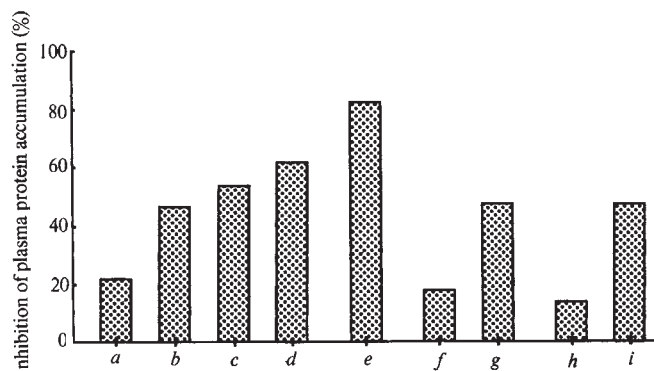
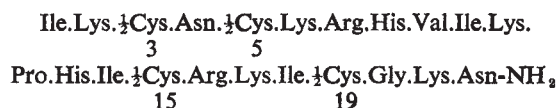


Fig. 2 Inhibition of plasma protein accumulation in turpentine oedema. Groups of five rats (♂, Wistar strain, histocompatible) received intravenous injection of 0.05 ml of ¹²⁵I-labelled rat serum albumin (~10 μCi mg⁻¹, 2.5 mg ml⁻¹) by the sublingual vein under light ether anaesthesia, and intra-articular injection of 0.01 ml of turpentine into the synovial cavity of the right knee joint. Anti-inflammatory agents were administered by intra-peritoneal or subcutaneous injection either at the time of, or 3 h before (steroids), turpentine and isotope injections. The animals were killed after 4 h, 1 ml samples of blood collected by cardiac puncture and the entire knee joint region of each hind limb removed by a wad punch (diameter 23 mm). The samples were counted in an automatic γ-spectrometer. Division of the specimen counts by the corresponding blood count gave their albumin content in terms of equivalent blood volumes. Subtraction of the albumin content of the left (uninjected) knee joint from that of the right (injected) knee joint gave the extravascular plasma protein accumulation which is a measure of the inflammation. The reduction by anti-inflammatory agents is expressed as a % inhibition. The non-steroidal anti-inflammatory drugs used were: a, mepyramine maleate, 5 mg kg⁻¹; b, indomethacin, 5 mg kg⁻¹; c, phenylbutazone, 50 mg kg⁻¹; d, sodium salicylate, 500 mg kg⁻¹ and, e, peptide 401, 2 mg kg⁻¹. Steroidal anti-inflammatory drugs used were: f, ACTH, 1 U kg⁻¹; g, dexamethasone, 25 μg kg⁻¹; and the mast cell degranulating agents; h, melittin, 2 mg kg⁻¹ and, i, 48/80, 2 mg kg⁻¹.

by them to have powerful mast cell degranulating activity. It contains twenty-two residues^{7,8} and the primary sequence is:



Essentially, by using tryptic hydrolysis combined with a single Edman degradation step followed by isolation and identification of the resulting peptides, we have shown that two disulphide bridges connect positions 3 to 15 and 5 to 19 respectively.

Anti-inflammatory activity was lost after treatment with trypsin and also after reduction of the disulphide bridges followed by carboxymethylation. The reduced peptide which had not been carboxymethylated was, however, still active, probably because of spontaneous reoxidation *in vivo*. With adrenalectomized animals the observed reduction in oedema remained virtually unaltered. The anti-inflammatory activity of peptide 401 is, therefore, presumably not mediated by the release of endogenous steroids or catecholamines.

We have also used increase in vascular permeability as a measure of inflammation⁹. Animals were injected with Evans blue dye and ¹²⁵I-albumin and inflammation was induced either by subplantar injection of carrageenin or intra-articular injection of turpentine. A comparison of the effects of peptide 401 with those produced by other substances of interest is shown in Fig. 2. While the data are not sufficiently extensive to make reliable quantitative comparisons of activity, it is clear that peptide 401 is, particularly on a molar basis, a very powerful anti-inflammatory agent.

Peptide 401 degranulates mast cells⁶ and as, in the rat, this involves the release of histamine and 5-hydroxytryptamine, the peptide itself should possess inflammatory activity. It is possible, therefore, that its anti-inflammatory activity is a consequence of this. It was found that peptide 401 does indeed

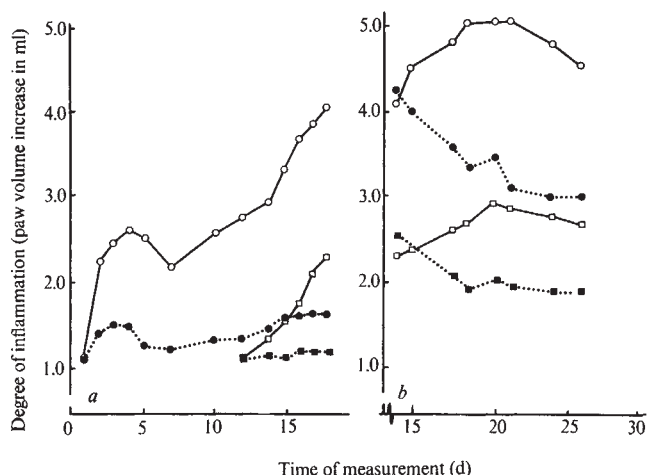


Fig. 3 Effect of peptide 401 on developing and established rat adjuvant-induced arthritis. Adjuvant arthritis was induced in groups of seven rats (δ Wistar, Guy's Hospital strain) by the injection into the right hind paw of 0.5 mg heat killed *Mycobacterium tuberculosis* (Central Veterinary Lab., Weybridge) finely dispersed in 0.1 ml liquid paraffin. The resulting inflammatory response was biphasic and was measured as the increase in volume of the hind paws. An initial reaction occurred in the injected hind paw which reached a peak on day 4. This was followed from 8 d onward by a second swelling in the injected hind paw and was accompanied by swellings in the contralateral uninjected hind paw, the fore paws, tail, ears and nose. The swelling which occurred in both hind paws is shown here for rats treated subcutaneously (1 ml/rat/d) with either peptide 401 (4 mg kg⁻¹ in saline) or saline alone (as control) both in, *a*, developing arthritis (treatment from day of injection of adjuvant until day 18) and in, *b*, established arthritis (treatment from day 14 to day 26 after adjuvant injection). Anti-inflammatory activity is seen as a failure to swell (developing arthritis) or a decrease in paw volume (established arthritis). $\circ$ — $\circ$, injected hind paw, saline control; $\square$ — $\square$, uninjected hind paw, saline control; $\bullet$ — $\bullet$, injected hind paw, peptide 401 treated; $\blacksquare$ — $\blacksquare$, uninjected hind paw, peptide 401 treated.

possess inflammatory activity. Intradermal injection in the dose range 1 to 1,000 ng produced increased vascular permeability, indicated by extravasation of ¹²⁵I-albumin. The effect could be totally abolished by pretreatment with mepyramine (2.5 mg kg⁻¹) and methysergide (2.5 mg kg⁻¹).

However, when injected subcutaneously at a dose of 1 mg kg⁻¹, peptide 401 prevented the blue dye permeability produced by intradermal injection of bradykinin (0.2 μ g), prostaglandin E₁ (5 μ g), serum kallikrein (100 μ g), histamine (0.3 μ g), 5-hydroxytryptamine (0.1 μ g) or compound 48/80 (0.025 μ g) providing that injection of the peptide was given about 1 h before the intradermal injection¹⁰. The delay is required because of slow absorption from the site of injection. Intravenous injection of much smaller doses (200 μ g kg⁻¹) immediately before intradermal injection of bradykinin, histamine or 5-hydroxytryptamine, prevented blue dye extravasation in each case. Furthermore, pretreatment of rats with mepyramine (2.5 mg kg⁻¹) and methysergide (2.5 mg kg⁻¹), which inhibit the action of histamine and 5-hydroxytryptamine, fully suppressed the skin reactions to these two substances. They did not, however, markedly affect the ability of peptide 401 to reduce the inflammatory effects, as judged by the extravasation of ¹²⁵I-albumin produced by intradermal injection of bradykinin, intra-articular turpentine or subplantar carrageenin.

Melitin also possesses mast-cell degranulating activity but was found to be devoid of anti-inflammatory activity in both the skin tests and the turpentine oedema test. Similarly, compound 48/80 which is known to be a highly potent mast cell degranulating agent, did not suppress the inflammatory response to intradermal histamine, 5-hydroxytryptamine or bradykinin even at high doses, although it showed weak anti-inflammatory activity in the carrageenin oedema test.

We conclude, therefore, that the anti-inflammatory activity of peptide 401 is not a result of its ability to lyse mast cells and

that the two effects reflect distinct pharmacological properties. Results consistent with this conclusion have been obtained (L. Bitensky, and J. Chayen, unpublished) using a new anti-inflammatory test^{11,12}, utilizing human skin, maintained in non-proliferative culture, treated with histamine (10⁻⁷ M). The anti-inflammatory activity of a given compound is then assessed by its ability to protect lysosomal membranes from damage produced by the histamine. Peptide 401 was found to be twice as potent (w/w) in this test as salicylate.

We have also tested peptide 401 in adjuvant arthritis in rats as it is thought that activity in this test correlates well with efficacy in treating human rheumatoid arthritis¹³. The results are summarized in Fig. 3. The inflammation associated with both the primary and secondary lesions in the established disease was considerably reduced by the treatment with peptide 401. The effects of starting the treatment at the same time as the adjuvant injection are much more dramatic, however, as the disease usually failed to develop.

It is of interest to ask whether peptide 401 could be responsible for the alleged curative properties of bee venom. The venom contains only small amounts of peptide 401 but much larger amounts of phospholipase-A and the peptides melitin and apamin, all of which are highly toxic¹⁴⁻¹⁷, and it does not seem very suitable as a therapeutic agent. Any beneficial effect would most likely arise from release of natural corticosteroids and there is some evidence in the literature that this occurs¹⁸. Nevertheless, the venom, long thought to possess anti-inflammatory properties, does contain a powerful anti-inflammatory agent the effect of which in man is still unknown.

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BOOK REVIEWS

Renaissance Science

Science, Medicine and Society in the Renaissance: Essays to honour Walter Pagel. Edited by Allen G. Debus. Volume 1. Pp. 275. Volume 2. Pp. 326. (Heinemann: London, May 1973.) £12 the set.

DR WALTER PAGEL is, without doubt, the most outstanding historian of medicine in Britain today. In order to honour him on his seventy-fifth birthday, friends and colleagues have gathered together a *Festschrift* under the editorship of one of his pupils, Dr Allen G. Debus, who is Professor of the History of Science in the University of Chicago. That a historian of science should take on this task is altogether appropriate, because Dr Pagel's work is as important for the field of the history of science as it is for the history of medicine.

Dr Pagel's father was the renowned German historian of medicine, Professor Julius Pagel of the University of Berlin, from whom he inherited his brilliance and love of history. After the rigorous German *humanistische Gymnasium* education he studied medicine and graduated in 1922. Hereafter, his life was divided between Germany and England, for he and his family came to this country in 1933, and between pathology and the history of medicine. It is remarkable that one man should achieve such distinction in two fields of medicine, for Dr Pagel's writings on pulmonary tuberculosis are as important as those on the history of medicine. In fact, he is often mistaken for two individuals, pathologist and historian!

The approach adopted by Dr Pagel to medical history has always been that of the scrupulous, dedicated scholar who wishes "... to interpret the facts of medical and scientific history 'as the outward expression of their time' ...". (Volume 1, page 7). Although his training and background have been in the Germanic tradition of pure history of medicine with few links with history or history of science, his published work, which comprises some four hundred and fifty items, together with his methodology, have influenced historians of science and of the Renaissance. His main interests have been in the sixteenth and seventeenth centuries, involving some of the most complex individuals and developments in the whole field of medical history. Thus his evaluations of Paracelsus (1493–1541) and Jean

Baptiste van Helmont (1577–1644), men who are as important to the history of science as to the history of medicine, have been classic and, fortunately for us, they are still appearing. The remarkable series of papers on William Harvey (1578–1657) and the recent book on his biological ideas testify to Pagel's astonishingly deep understanding of sixteenth and seventeenth century science, medicine, religion, philosophy, mysticism, education and many other aspects of culture in general. Nor have his interests been restricted to this period, for he has written on eighteenth and nineteenth century medicine too.

It is therefore fitting that the contents of these commemorative volumes should reflect all these facts, Dr Pagel's historical approach, scholarly methodology, and his chief interests. There are no less than thirty-eight papers from six countries and apparently these numbers could have been larger and the spectrum of topics wider, although still within his sphere of interest, had it proved possible to include papers from all who wished to contribute. Each essay is brief, scholarly, well written, and documented impeccably; the writers have made sure that the style and content of their compositions mirror Dr Pagel's rigorous standards. They cover a variety of subjects in both the history of medicine and science but they can mostly be grouped into those dealing with special aspects of the Renaissance and of the 17th century, with Paracelsus, the Paracelsians, or chemical medicine, and with Harvey or the circulation of the blood. The volumes, therefore, cover a wider period of time than the title would suggest. There is a biographical introduction by Professor Debus, a bibliography of Dr Pagel's writings, a brief account of each contributor, but no index. Naturally enough this book will be of wide appeal, for historians of science, of the Renaissance, of the 17th century, as well as of the history of medicine will find in it several items of value to their own studies.

On the whole, the *Festschrift* tends to be very uneven in content and style, and although important papers are to be found in them, often there are many of small importance. This example, however, is an exception, and the editor together with his contributors are to be congratulated on their inspired efforts expended in producing not only a lasting record of their regard and affection for Dr Pagel but a monument of scholarship

dedicated to "... a very kind and gentle man and to a magnificent scholar", as Dr Debus appropriately styles him (Volume 1, page 8).

EDWIN CLARKE

Inorganic Biology

The Inorganic Chemistry of Biological Processes. By M. N. Hughes. Pp. 304. (Wiley: New York and London, December 1972.) £4.50.

THE recognition that metal ions play a very important role in biological systems has been a great stimulus to inorganic chemists. It has provided scope for speculation generally safe from too rigorous testing against real systems, and for the preparation of model systems based upon whatever aspects of a given biological system seem (subjectively) important to the researcher. It has also spawned a variety of interdisciplinary activities, some of which achieve identity through being named, and "biological inorganic chemistry" is one such.

This book aims to be an introduction to biological inorganic chemistry for teachers and advanced students. In about 300 pages of text it attempts to give a background to modern transition metal complex chemistry, to review the techniques of studying metalloproteins, and to describe the main enzymic functions in which inorganic ions appear important: hydrolytic metallo- and metal-activated enzymes, redox systems, nitrogen fixation and oxygen carriers. The book closes with two shorter chapters on alkali and alkaline earth ions in biological systems, and the use of metal ions and chelating agents in medicine.

The author has set himself an immense task. The amount of condensation and compression needed to achieve it requires writing of a very high standard, and it cannot be claimed that he has consistently reached it. Indeed, the almost inevitable result is a degree of compression and generalization which makes many of his statements of little value to students and comprehensible only to those already familiar with the material. Thus (page 17) "the presence of calcium ions results in the activation of certain enzymes and hence muscle

contraction", or (page 24) Cu(II) is a transition metal ion, whereas Cu(I) is not, or (page 35) "the spin-orbit coupling is very important in determining the detailed magnetic properties of many transition metal ions", or (page 49) "For inorganic complexes g -values are higher than 2. The anisotropy of the g -value can give much information"; and "The position of the Etr resonance gives the field at which it occurs". There are also occasional errors, the most glaring from the point of view of a chemist being the implication that the d -orbitals of a metal in a tetrahedral complex are split into t_{2g} and e_g sets.

This selection of examples is taken from the first section of the book, which manifestly cannot be recommended. The subsequent discussion of metallo-enzymes, though sometimes stodgy, provides much useful information to the judicious reader. There are more than 500 references, and some indication of those which are more appropriate to students would have been useful. I doubt whether biological inorganic chemistry is yet a discipline in its own right and a satisfactory textbook has yet to be written. This volume is not more than a brave attempt.

G. J. LEIGH

Neural Biology

Nervous Systems. By Peter N. R. Usherwood. Pp. v+122. (Edward Arnold: London, April 1973.) £2.80 boards; £1.40 paper.

THE author's choice of contents for this book reveals how he reflects our times by presenting a standard account of the electrochemistry of the nerve impulse with a fairly detailed account of conduction and synaptic transmission but with a hotch-potch of physiological examples and anatomy to try to illustrate how nervous systems actually work. To be given the nerve impulse in such detail is bound to be puzzling to students when the whole point about the nervous system is the way in which the elements interact with each other. A fault is that the anatomy in this book is mainly the gross external shapes of ganglia: lack of space is no excuse, for most of the illustrations could have been drawn as composite pictures and to fit the page width. A whole page to show the position of a frog's tympanum is only one of eleven illustrations on hearing in a book that is pinched in other ways. Numerous examples, as in much scientific work, show that the author received inadequate critical comment on the manuscript. It is misleading to suggest, for example, that synapses resemble the remarkable scanning electron microscope picture of a molluscan ganglion which so far as I know never

proved repeatable. Other minor errors of judgment are easily overlooked, for example, that the mnemonic is an elementary memory unit of the octopus optic lobe: it is an idea relevant to many learning studies but, for some strange reason, in favour mainly with a few who study molluscs. To be non-critical in a section on RNA in a chapter on memory could again be misleading at this level, and to accept axon flow in addition to axoplasmic flow could be contentious.

The main teaching problem in this subject at present is to promote understanding of neurone interactions as causes of perception, of movement control and so on. This book shows something of the structure of the nervous system at gross and at electron microscope level, but little about its essential nature as a communicating system. It certainly does not convey how behaviour has its basis in the choice of which neurones are active. It illustrates sense organs and their action but not pattern abstraction: it details the processes at synapses but fails to follow up with the marvels of integration that are explained by the synaptic mechanism.

The mechanism of origin and the importance of the frequency code seem to have been forgotten, but a great compensatory feature is that the book is written with enthusiasm. Finally, an essay topic for extreme optimists is the final suggestion of the book, that maybe we shall even know all there is to know about that enigmatic structure the human brain.

G. ADRIAN HORRIDGE

Organic Chemistry

Organic Reaction Mechanisms, 1971. Edited by B. Capon and C. W. Rees. (An Annual Survey Covering the Literature dated December 1970 through to November 1971.) Pp. x+648. (Wiley Interscience: London and New York, December 1972.) £16.

THIS is the seventh in a series reviewing annual progress in the study of mechanisms in organic chemistry. The field is covered in fourteen chapters written by thirteen authors and is interpreted in a fairly broad manner, with a chapter on photochemistry, and extensive references to enzymic catalysis, to organometallic systems, and to structural information on species related to reaction intermediates. The aims of the book are thus similar to those of the Specialist Periodical Reports of the Chemical Society, which does not have a title in this area at present, presumably because of the success of the Capon and Rees series.

Comprehensive literature coverage is claimed (almost 5,000 papers were scanned for this volume) and the authors provide brief exposition and comment on the papers they consider interesting and important. The value of a book like this depends on two things: (a) the quality of the exposition and comment on individual papers and (b) the ordering and juxtaposition of material to bring out relationships between different pieces of work. On the first count this volume seems to be excellent. I can find very few examples where the main import of a paper has been missed. On the second count the degree of overlap and of cross referencing seems to me to be about right in general. The chapters divide the subject up in a simple and natural way, though there is perhaps a little more overlap between the first two chapters on "Carbonium Ions" and on "Nucleophilic Aliphatic Substitution" than is necessary. In one or two places the organization is beginning to show signs of age in preserving emphasis on matters which were of great interest in 1965 but have perhaps faded out now. The cumulative index is a very valuable feature.

In all, a good volume in an established series; the price is, of course, set for library purchase only.

R. W. ALDER

Chemistry of Surfaces

Surface Chemistry and Colloids. Edited by M. Kerker. Consultant editor, A. D. Buckingham. (MTP International Review of Science.) Pp. 306. (Butterworth: London; University Park: Baltimore, 1972.) £10; \$24.50.

THIS book is volume 7 of the series (Series One) on physical chemistry, which in all comprises thirteen volumes plus an index volume. Similar series on inorganic chemistry and organic chemistry are either now available or in preparation. All are reviews and deal with the period 1967-1971; the whole venture is to be repeated in 1974. Thus there is considerable similarity in aim with *Annual Reports of the Chemical Society*.

This volume contains eight chapters of varying length, contributed by authors from all parts of the world, and covering broadly both surface chemistry and colloids. Short chapters on "Insoluble Monolayers" (by G. L. Gaines), on "Recent Advances in the Study of Solid Surfaces" (by W. P. Ellis) and on "Chemisorption on Tungsten Crystal Planes" (by H. Wise) occur, but much longer contributions on "Membranes: their Interfacial Chemistry and Biophysics" (by H. Ti. Tien) and on "The

Physical Adsorption of Gases" (by S. J. Gregg) are included. Colloids are represented by three long contributions: "Aggregation in Surfactant Systems" (by Per Ekwall, I. Danielsson and Per Stenius), "Theory of Homogeneous Nucleation from the Vapour" (by G. M. Pound, K. Nishioka and J. Lothe) and "Hydrosols" (by D. H. Napper and R. J. Hunter). Each contribution is well provided with references (mainly very recent) and a comprehensive list of headings of sections and subsections. The latter will be much used since no subject or name index for the volume is included, indices for the series being collected in the index volume.

The choice of topics would seem at this time to be wise but undoubtedly will require modification in further volumes. Some of the shorter articles are considerably condensed and designed for the specialist rather than the new worker in the field, but, on the other hand, the chapters on membranes and surfactants are of more general character and more suited to the general reader. The final 60-page chapter on hydrosols is a comprehensive advanced treatment, which includes the preparation and characterization of dispersions, double layer theory and colloidal stability as well as coagulation.

The book is adequately produced with clear diagrams, but its price will ensure that it occurs mainly on institutional library shelves. P. JOHNSON

Properties of Metals

Solid State Theory in Metallurgy. By P. Wilkes. Pp. xii + 453. (Cambridge University Press: London, 1973.) £8.95; £3.20 paper.

THE modern student of metallurgy no longer sees his ultimate goal as "the art of working metals", to quote the dictionary, but is more akin to the physicist, or "student of nature", to quote the same source. He seeks a more basic understanding of the properties of metals and solids which make them useful to mankind, and consequently the knowledge of both the electronic and atomic structure of condensed matter is of profound importance in his studies. In a past era the area of electronic structure would normally be considered the domain of the solid state physicist, but it is encouraging to review a new book on solid state theory by a metallurgist aimed at undergraduate and graduate students of metallurgy and material science.

Dr Wilkes's book is divided into three parts. The first two parts are written so that they can be studied concurrently

or independently whilst the final part draws upon the results of the previous sections. In part I, starting from the physics of the free electron, Dr Wilkes develops ideas on the behaviour of free electrons in a solid in a logical, if conventional, manner. In part II the concept of the crystal lattice is described. Lattice vibrations in, and the elastic properties of, such an idealized solid are described and compared with the properties of real materials. Lattice defects and faults are then introduced, but not dwelt upon over-long since this area is amply covered in other metallurgical texts.

There follows a section on diffraction by crystals which not only describes the theory and experimental techniques available (X rays and electrons are mentioned but, annoyingly, not neutrons) but, using Fourier methods, clearly shows that the underlying connexions between diffraction and the Brillouin zone theory are solids. This, to me, is the best section in the book.

In the final part, the theory and properties of electrons in real metals are explored through the nearly free electron and tight binding methods, introducing the ideas of pseudopotentials, pair potentials and screening on the way. The ultimate usefulness of the theory is now made evident by comparison with the structure and properties of a range of metals, semiconductors and alloys. In the final chapter the theory is applied to high energy electrons in a lattice and the consequences in electron microscopy and diffraction.

The book is written in an exciting style of new discovery indicating its obvious kinship to the lecture course which the author no doubt gave at Manchester. The text is generally well illustrated by a series of informative diagrams and photographs and each chapter ends with a comprehensive list of books for further reading though, unfortunately, there are no references to original articles or papers. Dr Wilkes says in the preface that he has endeavoured "to explain each mathematical step and omit none"—a worthy aim for an undergraduate text which is faithfully maintained throughout the book. The mathematical steps do occasionally, however, hold up the pace of the physical argument. Perhaps more mathematical appendices would have helped, but this is a minor criticism.

The level of the material presented in parts I and II should not present difficulties to first and second year undergraduate students, but some sections of part III are clearly postgraduate material. The question might then be raised as to whether any one book can satisfactorily aim at such diverse levels of experience. I believe that with guidance the able undergraduate should not find himself "out of depth" with the majority

of this text, and many postgraduate metallurgists will find the book a clear introduction to an unfamiliar area of knowledge.

Taking into account the minor reservations and criticisms I have made, I still feel that the book can be strongly recommended to students of metallurgy and material science, and would make a worthwhile introduction to solid state physics for students of other disciplines.

L. GILLOTT

Scattering Theory

Quantum Theory of Scattering Processes. (International Encyclopedia of Physical Chemistry and Chemical Physics.) By J. E. G. Farina. Pp. xi + 152. (Pergamon: Oxford and New York, February 1973.) £4.50.

THIS short and lucid book provides a sound introduction to the quantum theory of collisions for research workers in physics, chemistry and mathematics. Compactness has been achieved by concentrating on a small number of fundamental topics, which are illustrated with examples drawn from atomic physics. The compassionate author carefully explains each step in the algebra and even the more difficult chapters should be easily followed by a first year graduate student. Although it is necessary to abandon rigour occasionally in a book of this length, the author points out such shortcomings where they apply and his mathematics is conscientiously scrupulous in most of the text.

The introductory chapter of the book deals with the properties of important differential equations arising in collision theory and solves the problem of scattering by a centre of force using partial wave analysis and the Kohn variational method. In chapter 2 the Born series is derived *via* the free particle Green's function and the integral equation of scattering. Chapter 3 tackles problems raised by the Pauli principle and the separation of relative and centre of mass motion. Inelastic scattering and rearrangement collisions are considered in the next chapter. The fifth chapter, on formal scattering theory, begins with a treatment of some useful contour integrals and uses the results to derive the Lippmann-Schwinger equation, which is then applied to direct collisions and the scattering of a particle by two centres of force. The remaining chapters are concerned with the time dependent approach to collisions and the scattering matrix.

The fundamentals of the subject are treated thoroughly in this admirable book, but the coverage is not extensive enough, even at an elementary level, for

most requirements. Nuclear physicists will be particularly affected by the failure to consider particles of non-zero spin and observables other than cross-sections, at a time when the proliferation of polarized sources has made asymmetry and triple scattering measurements commonplace. I know of no other work on this subject which can be read from end to end in a sensible time, however, and as such it is the most suitable book for a beginner.

V. R. W. EDWARDS

Practical Thermodynamics

Macroscopic Thermodynamics. By J. S. Turton. Pp. xvi+300. (Wiley: London and New York, April 1973.) £5.50 cloth; £2.95 paper.

HERE is an excellent introductory textbook on engineering thermodynamics to swell the contents of an already well stocked shelf. Of course, none of this classical material is new and the contents can be found in a number of other similar textbooks so it is inevitable that we should ask what the present author and printer together have achieved.

The strength of this textbook lies in a combination of the clarity of the author's style, his decision strictly to limit the contents to that part of thermodynamics which is relevant to the treatment of power cycles, refrigeration cycles and heat engines and to his inclusion of more than eighty fully worked examples in which both SI and British units are used. In addition more than 100 problems are included along with their answers so that a student who works carefully through the book will emerge with an ability to deal with a variety of both numerical problems and others requiring an understanding of the logic of thermodynamics.

The printing and layout are impeccable and the clean idealized diagrams give the book a real feeling of space, unlike some of its competitors which tend to be rather cramped. In order to achieve this open appearance in a book of this length some of the topics usually dealt with at this level have been omitted. There is no discussion of heat transfer by conduction, convection or radiation, nor is there any mention of the jet engine, although some of the principles involved appear in the chapter concerned with the combustion of fuels. The more recent technologies of direct energy conversion using semiconductors, MHD and fuel cells have also been omitted in order to give a more complete treatment of reciprocating machines.

Unexpectedly the International Prac-

tical Temperature scale is described in some detail, while in the same chapter the diagram illustrating a thermocouple circuit makes the usual mistake of showing only one ice point junction, although two dissimilar metals are shown (for example, Pt-Pt, Rh or Chromel-Alumel).

Nuclear fuels and solar energy are regarded as being outside the scope of the book, and it seems to look forward optimistically to an undiminished supply of fossilized fuels. When at last the supplies of these conventional fuels begin to decline how will the new textbooks on engineering thermodynamics respond?

Within the chosen range of contents the author has produced a first-class competitive textbook which will soon find a place in university mechanical engineering courses.

J. C. MATTHEWS

Lichen Alarm

Air Pollution and Lichens. Edited by B. W. Ferry, M. S. Baddeley and D. L. Hawksworth. Pp. x+389. (Athlone: London, April 1973.) £6.25.

THERE is a good deal to be said for using a biological method for estimating air pollution; and for this purpose lichens have certain advantages, such as their simple structure, slow growth, mainly airborne nutrition, and ability to absorb, passively, almost anything in air or water which comes in contact with the thallus. Thus, though resistant to harsh conditions of minimal nutrition, temperature, and water loss, most lichens are unusually sensitive to the accumulation of phyto-toxic materials.

These facts have been known to lichenologists for over a century, so it is perhaps surprising that this is the first book on the subject, but quantitative work has had to wait for the present flourishing condition of lichenology, and for the regular and widespread monitoring of at least one of the major air pollutants, namely sulphur dioxide. As might be expected, therefore, most of the book is concerned with SO₂ and its effects. It is a collection of seventeen papers, mainly of a review type, by a total of nineteen authors, several of whom appear more than once. Most of them might be described as leading members of that very active body, the British Lichen Society, although three are from Canada, two from the USA, and one from Belgium.

After a short introduction by P. W. James, P. W. J. Saunders and C. M. Wood review at some length the production, dispersal and fate of SO₂ in

the environment. In those later chapters which deal with the recording and mapping of lichens, their distribution is assumed to relate to this one among the pollutants. Britain is probably better provided with recording gauges for SO₂ than any other country (about 1,300 in 1968) and this has enabled British workers to devise two biological scales for estimating SO₂ levels, which are already proving their worth. These are O. L. Gilbert's, based on bryophytes as well as lichens on several substrates, and Hawksworth and Rose's, which uses tree-bark lichens, both published in 1970. There are also in use several more complex, numerical indices of atmospheric pollution (IAP) or of poleotolerance (P) devised in Belgium (De Sloover), Canada (LeBlanc *et al.*) and Estonia (Trass) but these do not seem to give more reliable results than the simpler British scales. Possibly Barkman's three lichen-based categories of light, moderate and heavy pollution for central Linburg (Belgium), which were used in planning the location of housing and industry, may be of the most practical use.

In chapter 7, B. J. Coppins sets aside the "drought hypothesis" of J. Rydzak; but though there is little doubt that "toxic gas" is the main influence, humidity is always an important local factor; and in the longest of several chapters on lichen physiology (chapter 12) J. F. Farrar sounds a note of caution, stressing the many variables, besides SO₂ levels, which may affect the growth and survival of lichens.

Some of the other pollutants—fertilizers, sprays, weedkillers, radioactive nuclides, heavy metals, smoke—are dealt with by P. W. James in chapter 8, but there is little or nothing known about the effects on lichens of ozone, H₂S, or the car exhaust gases. There is one chapter by O. L. Gilbert on fluorides, which are increasingly used in industry, but we are told several times in the book that their effects are merely local, which seems doubtful, as no monitoring has been done except around a few smelters and so on in rural areas.

The historical changes in the lichen flora of England and Wales, outlined in chapter 16, give us an interesting picture of the growth of pollution; and the final chapter is a summary of the book, with suggestions for future work, for which, indeed, there is immense scope. There is a good index, and ample references at the end of each chapter. The editors might, perhaps, have pulled the collection together a bit more, but it is a pioneer work which is likely to remain essential not only for lichenologists but for the far wider readership of those who, nowadays, have an interest in the quality of the air we breathe.

C. G. DOBBS

INSTRUMENT REVIEW

Measuring NQR Spectra

Nuclear Quadrupole Resonance (NQR) Spectrometer. (Decca Radar Limited, Instrument Division, Lyon Road, Walton-on-Thames, Surrey, from about £6,275.)

Nuclear quadrupole resonance spectroscopy is a branch of magnetic spectroscopy in which certain nuclei absorb energy from radio waves. The energy levels arise from the interaction of a nucleus that has a non-spherical charge distribution (that is, nuclear spin quantum number $I > \frac{1}{2}$) with electric field gradients within the molecule. Thus an NQR spectrometer does not involve a magnet because the internal electric field gradient in NQR fulfils a similar role to the external magnetic field in NMR. The energy of interaction between a quadrupolar nucleus and the electric field gradient is proportional to the nuclear quadrupole coupling constant¹.

Nuclear quadrupole coupling constants can be measured by several techniques such as molecular beam magnetic resonance in the gas phase and by NQR spectroscopy in the solid state². NQR spectrometers fall into two groups. First spectrometers, such as the present instrument and one manufactured by the Wilks Scientific Corporation (South Norwalk, Connecticut), which are designed to measure frequencies and if possible line shapes with the maximum sensitivity³; such instruments should be capable of scanning wide frequency ranges. The second group⁴, such as the Bruker spectrometer, measure the way in which the system responds to bursts of radiofrequency power, and so give information on the relaxation properties of the nuclei. Such information is more specifically of interest to the physicist whereas the chemist is more concerned with the determination of NQR frequencies, and hence coupling constants, which he can use (i) to investigate solid-state effects such as phase-transitions, molecular point-symmetry and other lattice effects⁵; (ii) to fingerprint a molecule (such as an organic molecule) by comparing the frequencies observed in an unknown with those of standard compounds⁶; (iii) to calculate approximate electron distributions within molecules⁷. The Decca instrument is designed principally for the chemist.

Nuclear quadrupole resonance spectroscopy can only be carried out using crystalline samples where the electric

field-gradient axes are fixed in space. In a liquid, molecular vibrations modulate the electric field-gradient and induce transitions between quadrupole levels to such an extent that the lifetime of the quadrupolar state becomes so short as to cause uncertainty broadening, making the line too broad to be detected. Although NQR spectroscopy is in theory applicable to gases, quadrupole coupling constants in the gas phase are more easily determined from microwave pure-rotation spectra².

The NQR technique is not, and probably never will be, as simple as other spectroscopic techniques such as infrared and NMR. Thus because signals are weak it requires slow scanning rates, which in turn means that it takes a long time to locate a signal. At present it is almost impossible to predict when a given resonance will be strong, weak or unobservable, and samples in the last two classes can take up a lot of time. To help the potential customer Decca will run a trial sample for him to help evaluate the potential use of NQR.

As I do not own a Decca NQR spectrometer I familiarized myself with the instrument by following the instruction manual to record the spectra of *p*-dichlorobenzene, CCl_4 , *N*-chlorosuccinimide and Sb_2O_3 . In each case I obtained the literature spectrum fairly readily although the cross-referencing in the manual is poor; cross-references are generally to a chapter rather than to the specific page. In addition I found two of the controls labelled "P.S.D. Set" and "Internal F.M. Amplitude" on the spectrometer had different names in the manual ("P.S.D. Gain" and "Attenuators" respectively). In order to set up both the Sideband Suppression and the Frequency Marker it was necessary to read the relevant chapters through twice before proceeding. The lack of a clear stepwise procedure for setting up both controls meant that when I did proceed it was with some trepidation, although I was assured that it was virtually impossible to cause damage by misusing the controls and to be fair the manual did contain all the information required. Once mastered the Sideband Suppression and the Frequency Marker worked well. Although setting up the Sideband Suppression can be achieved without an oscilloscope, Decca warn that it requires practice. Personally I found that even using an oscilloscope it presented something of a challenge for the first couple of days.

In following the manual I quickly

established that the spectrometer achieved all that the manufacturer claimed for it. In addition I tested it with a number of transition metal chlorine complexes. For example, with K_2PtCl_6 the present spectrometer gave a signal at 17.95 MHz with a signal-to-noise ratio of 3:1 as compared to 0.8:1 reported in the literature⁸. When searching for an unknown signal it is vital to scan very slowly, preferably overnight. This, of course, requires a considerable measure of stability within the instrument to avoid the recorder going off-scale and thus failing to record the spectrum. Although there is some baseline drift its magnitude can be checked manually in advance so that overnight and even over-weekend runs are possible. This is a very important point in favour of the present instrument.

The final design of any spectrometer is inevitably the result of a number of compromises. Although the final appearance of the Decca instrument is very pleasant there are a number of features that could have been improved.

First, to change the coils involves lifting up the oscillator unit and placing it on its side which is not only a tricky operation but requires a measure of strength. Perhaps a vertical jack could be fitted?

Second, to minimize heat losses the probe is supported on a thin coaxial line which will buckle easily. On several occasions I found it very difficult to align the threads necessary to screw this coaxial line on to the oscillator unit, and the risk of buckling was thus enhanced. The short probe (for 75 to 90 MHz operation) is even more difficult to fit on account of the small space left around the collar that retains it.

Third, there are many cable connexions at the back of the instrument. They are located there to be out of the way and give a pleasant appearance to the spectrometer, but on occasion one must reach them, which is not simple. There is also the possibility of a connexion coming apart accidentally and not being noticed—at one stage I spent half an hour trying to find why the marker unit was not working, only to find that its plug had fallen off (how I do not know). Locating the plugs on the side or the top of the spectrometer might be more valuable in operation although aesthetically less pleasing.

The modular nature of the spectrometer should make servicing relatively simple as Decca will exchange units

during repair. Beyond this, detailed circuit diagrams are provided to help the customer with electronics experience to service his own instrument. The instruments in service have so far developed very few faults.

The instrument requires about 6 foot of bench space, although 8 foot makes it easier to get to the back of the spectrometer to reach the plugs and the scan speed control.

At present the instrument comes in one of two basic packages covering either 5.5 to 55 MHz or 8.9 to 90 MHz. Low frequency (1 to 10 MHz) and high frequency (90 to 350 MHz) attachments are being developed and should be available now.

The Decca instrument does an excellent job within the limitations outlined above as inherent in NQR spectroscopy. As mentioned above it is not yet possible to predict the intensities of NQR signals and accordingly the customer would be wise to submit representative samples to Decca who will record their spectra for evaluation. If suitable signals are obtained I can strongly recommend the purchase of this instrument.

F. R. HARTLEY

- ¹ Bronswijk, W. van, *Struct. Bond.*, **7**, 87 (1970).
- ² Lucken, E. A. C., *Nuclear Quadrupole Coupling Constants* (Academic Press, London and New York, 1969).
- ³ Smith, J. A. S., *J. chem. Educ.*, **48**, A77 (1971).
- ⁴ Smith, J. A. S., *J. chem. Educ.*, **48**, A147 (1971).
- ⁵ Brame, E. G., *Analyt. Chem.*, **39**, 918 (1967).
- ⁶ Fitzky, H. G., *International Symposium on NQR Spectroscopy*, paper 12 (London, September 1972).
- ⁷ Smith, J. A. S., *J. chem. Educ.*, **48**, 39 (1971).
- ⁸ Fryer, C. W., and Smith, J. A. S., *J. chem. Soc.*, **A**, 1029 (1970).

Errata

In the article "Unique Amyloid Protein Subunit common to Different Types of Amyloid Fibril" by G. Husby, J. B. Natvig, T. E. Michaelsen, K. Sletten and H. Høst (*Nature*, **244**, 362; 1973), paragraph 1, lines 7 and 8, should read "... a molecular weight of 8,500, named by us protein AS (amyloid subunit) ..." instead of "... a molecular weight of 85,000, named by us ..."

In the article "Transformation of Mammalian Cells *in vitro* by Low Doses of X Rays" by C. Borek and E. J. Hall (*Nature*, **243**, 450; 1973) the legend to Table 1 should read

$$**\text{Plating efficiency (P.E.)} = \frac{\text{Number of clones counted}}{\text{Number of cells plated}} \times 100$$

$$\dagger\text{Surviving fraction (S.F.)} = \frac{\text{Number of clones counted}}{\text{Number of cells plated} \times \text{P.E.}}$$

DUE to a printers' error the title of the article by M. G. R. Varma *et al.* (*Nature*, **244**, 452; 1973) was incorrect and should read "Zirga Virus, a New Arbovirus Isolated from Bird-infesting Ticks".

Corrigendum

In the article "Potent Pyrethroid Insecticides from Modified Cyclopropane Acids" by M. Elliott *et al.* (*Nature*, **244**, 456; 1973) two references should be added:

- ¹⁴ Crombie, L., Doherty, C. E., and Pattenden, G., *J. chem. Soc., C*, 1077 (1970).
- ¹⁵ Brit. Pat. 1,270,270 (to Roussel-Uclaf, S. A.).

and so refs 10 and 11 on Fig. 2 should be changed to 14 and 15 respectively.

Announcements

University News

Professor Jasper P. Brener, University of Tennessee, has been appointed to the second Chair of Psychology at the University of Hull.

Appointments

His Grace the Duke of Northumberland, KG, TD, FRS, has been appointed Chairman of the Medical Research Council from October 1973.

The following scientific appointments to the Medical Research Council have been made: Professor A. C. Dornhorst, MD, FRCP; Dr Helen Muir, MA, DPhil. Lord Halsbury, FRS, has been appointed as a lay member of the Council.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

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